REGIONAL ILEITIS

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By

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Preface

THE PROMPT ACCEPTANCE of the concept of regional ileitis by the profession at large has led, in the last few years to a wide and elaborate knowledge of the clinical aspects and surgical treatment of the malady. The literature on the subject extends over several hundred published references with a widespread distribution throughout the world.

To attempt to write the life history of a disease requires extended experience with its pathologic aspects, the intensive study of ample clinical samplings and a numerous and illustrative case material. Fifteen years is too short a period in the limited world of scientific and human experience to encompass more than a general concept of the life cycle of an entity. This is particularly true when the process of extension progresses most often slowly, and when intelligent recognition of the various stages becomes possible only after long and intimate association with the disease. However, by pooling the published observations of the many students in the field and by using such a vast data as a measuring standard with which to enlighten one's own more limited experiences the task of organizing the progressive story of a disease can be attempted with greater confidence.

The etiology of regional ileitis at least as to a specific causative agency remains unknown. The clinical concept and diagnosis and the roentgenologic recognition is well advanced and accepted. The surgical cure or attempts at cure are still in a state of flux. Whatever skepticism

occurs is related to the field of surgery where frequent disappointment has been experienced and criticism has been levelled Such scientific criticism is healthy and when constructive, can lead only to advance in thought and in practical knowledge

Least understood is the field of ileo jejunitis, that affection of the higher segment of the small bowel which is rapidly being explored, its inflammatory and deficiency manifestations tabulated and organized So too with the combined forms of ileitis and colitis which present a tangled skein of primary and secondary affects leaving much still to be studied

This offering, begun as a brief monograph, has developed into a book, not from verbosity, but because the extensive literature and many worthy contributions from students throughout the world have made the extension necessary as a recognition of the wide spread interest of internists and surgeons in a subject which advances daily

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1 General Considerations: Scope of Study

THE TERM "Regional Ileitis" was coined and created in 1932 to describe what was considered as a new pathologic and clinical entity, a clear cut disease affecting the terminal segment or segments of the small bowel characterized by a subacute or chronic necrotizing and cicatrizing inflammation. While the term regional ileitis is still the most popular denomination of the disease, many other descriptive names have been created by successive authors to cover new and expanding concepts of the anatomic and pathologic aspects of this malady. Terminal ileitis was the first term applied because in the original publication the first 14 cases were all restricted anatomically to the terminal 8 to 12 inches of the ileum. "Regional ileitis," however, denoted a more widespread distribution. "Regional enteritis" was suggested by Brown, Bargen and Weber; "chronic cicatrizing enteritis" by Harris, Bell and Brunn and by Cushway; "chronic ulcerative enteritis" (Corr and Boeck); "segmental enteritis" (Lewisohn) to denote both the tendency to scar formation and the more widespread anatomic distribution. "Ileo colitis" was suggested by Erb and Farmer and again by Colp to indicate the not infrequent involvement of the colon. To this concept must now be added "ileo jejunitis," the same pathologic process extended to include anatomically all of the jejunum continuously or segmentally; and finally "ileo colitis" or "colo ileitis," a term created to cover those combined cases where some

segments of the large as well as the small bowel are concerned

As originally described, regional ileitis or enteritis is a nonspecific inflammatory disease, one of the larger group of intestinal granulomata, a process affecting mainly young adults and characterized by an acute, a subacute and a chronic phase of necrotizing ulcerating and cicatrizing inflammation The disease is further marked by its tendency to fistula formation within adjoining loops of the small and large bowel, by external fistulas to the abdominal wall, by frequent rectal suppurative complications A disproportionate increase of connective tissue may and does frequently lead to intestinal stenosis and obstruction Clinically, the disease is featured by fever, diarrhea, loss of weight, a secondary anemia, and by the formation of an intra abdominal mass, constituted of and by approximated loops of inflamed intestine frequently joined together by internal fistulas The process regularly begins or stops at the ileo cecal valve, the exceptions to this localization being few in number The disease advances upward by "skip lesions" separated by healthy "skipped areas" It is a progressive lesion in many instances, slowly or rapidly advancing in others it will remain for twenty or more years strictly localized in the terminal ileum Recurrences of the inflammatory process after palliative or radical surgical procedures further characterize the process as an active, persistent and recurrent disease

Historical Background

Nonspecific granulomata of the alimentary tract involving mainly the large bowel have been recognized for many years The European medical literature has been replete with innumerable examples of such inflammatory masses located in large and small intestine some even in the stomach included in these descriptions undoubtedly are many instances of what we recognize now as typical ileitis or enteritis In 1813, Combe and Saunders reported before

the Royal College of Physicians of London "A Singular Case of Stricture and Thickening of the Ileum" To quote in part "The lower part of the ileum, as far as the colon was contracted for the space of three feet to the size of a turkey quill" John Abercrombie discussed pathologic states of the ileum and reported cases very similar to regional ileitis His description published in 1828 is instructive "A girl aged 13, about a year before her death (1814) began to be afflicted with pain of the abdomen and frequent vomiting The caput coli three inches along the ascending colon and the lower end of the ileum to the extent of about eighteen inches, was distended, thickened in the coats, externally of a reddish color and internally covered by numerous well defined ulcers varying in size from a diameter of a split pea to that of a sixpence" After a lapse of almost a century, the English literature again contained a case report by Moynihan in 1907 entitled, "The Mimicry of Malignant Disease in the Large Intestine

In the meantime, the German literature began rapidly to show an abundance of references to nonspecific granulomata of inflammatory nature Braun in 1901 quotes 5 cases mostly of traumatic or hernial origin and later quotes 25 more cases from the current periodicals up to 1909 By 1920, Tietze had collated 281 references on this subject including at least 2 cases of typical regional ileitis (Lowen and also Willman) The literature now increased apace Dalziel contributing an excellent article The discussions in the German publications show an increasing interest Korte 1921 Landois 1923 Konjetzny 1932 report cases the whole subject crystallizing with a paper by Fischer and Lurmann This paper included the description of three cases of typical regional or terminal ileitis and recognized and granted priority to the original publication less than a year previous in this country [66] The discussion before the German Congress and thereafter as amplified by the experience of such noteworthy surgeons as von Haberer Gisbertz Peters Anschutz Fenster and others

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recognized, tuberculosis, syphilis and actinomycosis were excluded by definition

Regional Ileitis [66]

From this large and general group of nonspecific granulomata of the intestinal tract a subspecies which was termed regional ileitis was isolated, a distinction which was possible because this group was characterized by a consistent anatomic distribution, a characteristic clinical course, a progressive life history, typical complications of fistula formation and obstruction, this group being amenable further to successful surgical interference. It is interesting to note historically the amplification of the original concept of terminal ileitis. The first report covered 14 cases of a typically characteristic disease involving only the terminal segment or segments of the ileum. Acute cases were included among those running the more easily recognized chronic inflammatory course. Shortly thereafter the involvement in some cases of the upper reaches of the ileum and all or part of the jejunum, as noted by Harris, Bell and Brunn led to the identification of ileojejunitis either as an extension or as a continuation of terminal ileitis or as a subgroup per se in which the involvement of the terminal segments of the small intestine was subordinated to the process higher up. The participation of the colon segmentally either by contiguity from the terminal ileum or by scattered areas of coincidental disease was first noted by Colp and by Crohn and Rosenak and led to the creation of still another subgroup termed "ileocolitis" (Crohn and Berg), a most confused and complicated pattern of involvement of ileum and varying segments of the large bowel. In this latest subgroup the ileitis is regarded as the parent focus of infection, the colonic involvement being secondary in *time and* extension

Three years after the first designation of regional enteritis as an entity Brunner was able to collect 267 cases

By 1925, American writers had become cognizant of the subject of nonspecific granulomata of the intestinal tract. Coffen 1925, Horsley (including two fine case descriptions of ileitis), an excellent study by Moschcowitz and Wilensky (including an admirable photographic reproduction of ileitis) of 4 cases of granulomata, of which one was typical of ileitis as we now know it. Mock in 1931 summarized the subject of infective granulomata, attributing most of these pathologic masses to some interference with vascular supply to a given tissue, resulting in local necrosis followed by a proliferative reparative tissue reaction. He considered trauma as the most common etiologic agent. His cases, many of them due to penetrating foreign bodies, diverticulitis, strangulated hernia, silk and metallic ligatures, involved the sigmoid, stomach, omentum, splenic flexure and in one case participation of the terminal ileum. Golob added one case, and Erdmann and Burt 5 more cases, 2 of which had typical involvement of the terminal ileum with intestinal obstruction and of internal fistulas from ileum to cecum. Finally, in 1933 Ginzburg and Oppenheimer reported a group of 52 cases of nonspecific granulomata of the intestinal tract, cases due to vascular disturbances, to herniation, to sealed off intestinal perforations and included several cases of the entity which had already been isolated and termed regional ileitis.

This large group of nonspecific inflammatory granulomata involved any or all parts of the alimentary tract and omentum. They formed masses often obstructive in nature, usually simulating in their clinical course the picture of a new growth. They were characterized by a piling up of granulation tissue with various stages of ulceration, necrosis and fibroblastic proliferative secondary reactions. The histologic process consisted of round cell infiltration, fibroblasts, connective tissue stroma and new blood vessel formation with the occasional occurrence of giant cells of unusual magnitude (Moschcowitz and Wilensky). Etiologic agents apart from trauma and foreign bodies were not

and its subsequent course has been traced Above all, prognosis has been learned and finally the medical and surgical approaches to therapy have been tried, some discarded newer methods apprehended The whole problem of recurrences has come to light and been observed and a rational method of recognition and treatment has been attempted

Scope of the Present Study

This study is an analysis of instances of segmental enteritis, cases which have been under my own personal office and hospital care during all or part of the last sixteen to eighteen years They have all been private patients who have been observed carefully, treated and subjected to continuous analysis including follow up during this period Some of these patients were included in the original group that constituted the first fourteen cases published in 1932 as terminal ileitis The remainder have been registered during all of the succeeding years, the last additions to the list having terminated approximately six months ago to allow for some if not adequate follow up (October 1947) Ward cases in hospitals are not included—those that are listed have been accepted only because they solicited treatment and were registered as personal patients even though the previous surgical or medical treatment had been administered elsewhere For purposes of analysis and study this larger group may be subdivided into four essential categories

1 Regional ileitis—the chronic form	222 cases
2 Acute ileitis	16 cases
3 Ileo-jejunitis	38 cases
4 Combined cases—ileitis with involvement of some segment of the large bowel	22 cases
Total	298 cases

All four categories represent types of regional or cicatrizing enteritis They are not distinct entities in fact, mixed forms are not unusual The identical pathogenesis and

from the literature, in 1939 Ravdin and Johnston catalogued 393 cases from current periodicals. Confirmatory reports from the English literature were not long in making their appearance (Jackman, Hadfield, Barbour and Stokes, Molesworth, Hurst and his co authors), as likewise from the Dutch literature (Groen and Pompen, Snapper, Pompen and Groen)

A dissident viewpoint was advanced by several writers who considered regional ileitis a clinical but not a pathologic entity because of the occurrence of the disease at various other areas of the intestines. Characteristic lesions involving the jejunum were shown in 2 cases (Harris, Bell and Brunn), of 18 cases reported from the Mayo Clinic in 1934 (Brown, Bargen and Weber) the ileum was involved in 9, the jejunum in 3, the terminal ileum and parts of the colon in 6 instances. Homans and Hass, while recognizing typical terminal ileitis, questioned the localization of the process and felt that the jejunum was more often involved than was then recognized. They thought that the appendix was possibly an important etiologic factor, they further remarked for the first time that the disease might have a predilection for Hebrews (Mixter). Meyer and Rosi emphasized the involvement of the mesentery particularly in fistula formation. Erb and Farmer emphasized the acute phase in children as it simulated appendicitis. Reichert and Mathes made the first suggestion regarding etiology, namely, experimental lymphoedema by blocking lymphatics. Goldfarb and later Kantor gave the first veritable description of the roentgen appearance of the disease, the latter terming the appearance of the disease in the terminal ileum as the "string sign." Actually considerable knowledge has been added to the original concept of terminal or regional ileitis in the last sixteen years. The anatomic and pathologic states have been extended to include the upper reaches of the ileum and all of the jejunum; opportunity has been afforded for studying the life history of the disease, its progression and extensions. Acute ileitis has been analyzed

and its subsequent course has been traced Above all, prognosis has been learned, and finally the medical and surgical approaches to therapy have been tried, some discarded newer methods apprehended The whole problem of recurrences has come to light and been observed and a rational method of recognition and treatment has been attempted

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2 Regional Ileitis—Etiology (222 cases)

REGIONAL ILEITIS is a nonspecific chronic recurrent granulomatous disease affecting mainly young adults, and characterized by a necrotizing, ulcerating, inflammatory process, one in which cicatrizing elements in the long enduring cases is an important feature. The terminal ileum is apparently the seat and origin of the pathologic process though the whole ileum may be involved. Typically the process rests at the ileocecal valve, transcending that barrier only exceptionally. The disease clinically is marked by a low grade fever, by abdominal pain, most frequently by mild diarrhea and by progressive loss of weight and a secondary anemia. The occurrence of an intra-abdominal mass is frequently noted. The most striking clinical feature is the formation of fistulas of ileal origin, these fistulas leading from ileum to the abdominal wall or from ileum to other loops of bowel or other hollow viscera. Rectal complications of a suppurative nature constitute a striking manifestation of the disease. The pathologic process is a progressive and enduring one lasting over the course of many years. Eventually intestinal obstruction and hemorrhage may intervene. Spontaneous cures are minimal but may occur; surgical intervention is still the therapeutic method of choice.

Etiology

The true causation of ileitis remains unknown in spite of diligent efforts to ascertain a bacterial or specific agency

pathologic histology is common to them all. But they differ sufficiently clinically and anatomically to merit their consideration as separate groups, each group has identifying characteristics, has its own life history and prognosis as well as its individual approach to therapy.

The largest group of 222 cases of ileitis comprises the bulk of the study and provides the greatest number of the classic variety of the disease in which the ileum, particularly the terminal segments of small bowel, are involved. The disease being one of low grade pathogenicity and chronicity requires that this group be regarded as chronic regional ileitis. In contradistinction, the acute cases have been separately considered because of their own identifying characteristics though some confusion will arise when attempts are made to separate true primary acute ileitis from acute exacerbations of chronic recurrent ileitis.

The group of ileojejunitis has been separately considered because the involvement of the whole or of most of the small bowel introduces new elements of clinical significance and misses many of the distinguishing characteristics of the terminal form. Its life history is different, its therapeutic approach is entirely singular, its differential diagnosis and prognosis call for a more novel viewpoint. The fourth category of combined ileitis and colitis is so confusing with so many cross elements and complications and is so difficult a problem in therapy, particularly its successful surgical treatment, that it requires its own generic consideration.

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ETIOLOGY

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as the factor in its initiation It is of first importance to exclude tuberculosis as the specific infecting agency Much confusion in the past evolved from the inclusion of cases of nonspecific ileitis within the category of hypertrophic ileocecal tuberculosis All resected specimens of ileitis have been conscientiously subjected to careful histologic study, to careful staining methods for the recognition of the Koch bacillus in cut sections, to cultures and animal inoculation

Material from the bowel wall of the ileum and from mesenteric lymph nodes in resected cases were inoculated into guinea pigs, rabbits and chickens and proved negative in 5 of the original cases Subsequently, whenever a suspicion of tuberculosis has arisen, the most careful procedures have been followed to eliminate the Koch factor as an etiologic agency When tubercle bacilli have been demonstrated in cut sections, or when guinea pig inoculations have been positive, the case has been considered as intestinal tuberculosis and has been excluded from the series Singularly this has been necessary only once during the eighteen years of study, with only one case of primary intestinal tuberculosis simulating ileitis Frazer and Haggar reported a case of regional ileitis resected, in which the mesenteric lymph nodes showed old caseating tuberculosis the specimen of ileitis itself was free of any evident invasion by the tuberculous process and was nonspecific granulomatous in nature by histologic study

Syphilis and actinomycosis, two specific infections that may involve the intestine have been excluded as an etiologic agency because of the fact that serologically syphilis and histologically actinomycosis are easily differentiated and excepted

Specific Agencies

Many authors have found various bacteria in cultures of tissues or in peritoneal exudates and have implied that these bacteria were the etiologic agents of the disease This occurred many times in the earlier publications after the disease was first described recent literature has made no

such claims and no such confutations Erb and Farmer in one case found in stained sections of the involved gut gram negative bacilli apparently of the B coli group By culture they obtained a similar organism from the ileal mucosa, mesenteric lymph glands, liver and bile In their comment on the finding Ravdin and Johnston point out that these tissue cultures were taken eight hours after death and that no specific agglutinations against the patient's blood had been essayed Ross has found similar bacteria in one case Mixter noted frequent mixed cultures in the chronic cases, but regained in one case an anaerobic streptococcus from the peritoneal fluid from the mesenteric lymph nodes and from the deep surface of the intestinal ulcerations Peters found the usual enterococcus of intestinal type in the cultures of superficial tissue but no bacteria in the sections of deeper tissue Jackman, in 2 cases of acute ileitis, was not able to demonstrate bacteria in the deeper layers of the resected specimens Others have found gram positive cocci in the submucosa (Konjetzny) enterococci in stool cultures (Fischer and Lurmann), aerobacteria aerogenes (Halligan and Halligan) Mailer found streptococcus viridans in two of his cases

These various observations are of interest but fail to give consistent findings which would regularly implicate a single causative bacterial agency Numerous attempts by staining and by aerobic and anaerobic cultural methods and by animal inoculations have similarly failed to discover a singular offending agency

A most serious attempt to investigate the bacterial etiology of the disease was made by Pumphrey at the Mayo Clinic Thirteen cases of granuloma of the bowel were studied 10 of which were typical regional ileitis Cultures were taken by sterile technic in the operating room from resected specimens and regional lymph nodes The specimens were macerated and planted in media such as blood agar eosin methylene blue plates, dextrose brain broth chick mash overlayed with paraffin and agar slants Many

organisms, gram positive and gram negative were recovered, none of which could be said to be predominant throughout the series. In no instance was he able to isolate an organism of the dysentery group. None of these bacterial cultures were consistently agglutinated by the serum of the patient from whom the culture had been obtained nor by the serum of other patients suffering from the same disease. Cultures from the throats of 2 patients with the disease yielded streptococcus viridans, the injection of these cultures into rabbits failed to reproduce the disease. Exhaustive studies for tubercle bacilli and for spirochetes were similarly negative.

Johne's disease in cattle has many resemblances to human ileitis in its anatomic configuration except that the former is regularly demonstrated to be associated with a specific micro organism the Mycobacterium johnei. Williams injected johnei subcutaneously into patients with regional ileitis and also into normal controls without establishing any causal relationship between ileitis and Johne's disease.

PROTOZOA

The entamoeba histolytica was implicated by Cori and Boeck on the basis of one case finding. However, the typical pathologic lesions of amebiasis were absent from other segments of the large bowel as is characteristic of amoebic infestation. No other authors in the literature have made similar claims. In other instances Trichocephalus dispar, Oxyuris vermicularis, Giardia lamblia and other parasites have been found in the stool examinations but never sufficiently consistently as to imply that their presence was the cause of ileitis.

Foreign bodies which play so large a role in granulomata of the intestinal tract such as fish bones, metal ligatures, *food residues, pits, fragments of bone, are absent from* cases of true regional ileitis or jejunitis. Large giant cells are regularly found in histologic sections of ileitis; these giant cells are not tuberculous or syphilitic in origin. They

are best explained on the basis of foreign body inclusions but the extraneous substances that give rise to such giant cells are not gross or material in substance. They are probably in some instances due to lycopodium spores from dustings of surgical gloves at a previous surgical intervention or are due to minute fragments of food detritus collected and secondarily caught in the ulcerated pockets of the mucosa.

Bacillary Dysentery

Felsen claims a common source of origin for a large percentage of the cases of distal ileitis, chronic ulcerative colitis and nonspecific granulomata. This concomitant agent is in his belief the Shigella dysenteriae. In a follow up of 400 cases of acute bacillary dysentery he found 29 cases of acute distal ileitis, 22 cases of chronic distal ileitis, 18 cases of combined chronic ileo colitis and 84 cases of chronic ulcerative colitis. His study includes a survey of the late end results of the epidemic of bacillary dysentery which occurred at Jersey City in September 1933. He gives 84 cases with high serum agglutinations against Shigella dysenteriae and eight with positive stool cultures. He describes particularly an acute dysenteric appendicular form with involvement of the small bowel and various types of mixed forms involving terminal ileum and colon. His classification and acceptance of dysentery is based upon agglutination titers of 1 100 and over except for the Sonne Duval type in which he accepts 1 50 as significant. Positive stool cultures were obtained in 10 of 70 cases examined.

The findings and implications of Felsen so often quoted in the literature may be variously criticized. The agglutination in the serum of patients against recovered organisms and against type laboratory cultures are today open to the criticism of nonspecificity. Too many cross and nonspecific agglutinations occur to allow definite laboratory and clinical conclusions. The small number of positive stool cultures (ten) recovered after an epidemic of acute dysentery is not significant for ileitis unless it can be cor

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roborated in cases of regional ileitis by successive investigators, in a sufficient number of cases, over a sufficient length of study. Bisgard and Henski recovered a dysentery bacillus from the urine and right kidney in a single case of regional ileitis. The identity of the organisms was established by fermentation and agglutinations against stock sera.

In our own series of almost 600 cases, and in the experience with the additional ward cases at the Mount Sinai Hospital over eighteen years, I can recall only 2 cases with a transient positive culture for the Flexner type of dysentery and only an exceptional case with high agglutinations against similar bacteria. In only one instance an agglutination of 1 320 against Hiss was reached.

While one may accept the comment of Felsen that a type of disease similar to acute distal ileitis may occur during epidemics of bacillary dysentery and that occasional very exceptional instances of positive cultures or high titer serum agglutination may be observed, the imputation that regional ileitis or ileo jejunitis is regularly caused by the Shigella dysenteriae has not been substantiated and is not acceptable to most authors other than himself.

VIRUSES

The virus of lymphopathia venereum has been suggested as the cause of ileitis. Stafford in 10 cases of lymphopathia venereum, found 3 suffering from a form of segmental colitis, in no case was the small bowel involved. Because of the cicatrizing tendencies and the possible similarity to cicatrization found in the rectum in lymphopathia venereum, Koster and his associates carried out the Frei test in 4 cases of resected ileitis and in 2 others of ileitis not resected with negative results. Rodaniche, Kirsner and Palmer considered *that the two diseases resembled each* other in the primary lymphatic involvement and later development of severe stenosing lesions. However, in 4 cases of ileitis, the Frei test was negative with mouse and human

antigens The serum was also found negative for neutralizing antibodies against the virus Similar negative results were found by Friedl Meyer However, Llombart and Mayern described a case of lymphopathia venereum with multiple strictures of the ileum as well as a rectal stricture The terminal ileum and the cecum were marked by elate lane like beading, the lesion extending down to the submucosa and even to the muscularis Ocular manifestations were also present, confirmatory of the virus type of infection Coutts and Oporo in a study of several cases of lymphopathia venereum were able to demonstrate only one instance with ileal involvement In this person there was an extensive proctitis and an ileitis involving a large part of the terminal ileum

Likely and Lasa report in detail, in a Negress bearing the obvious perineal and vulval lesions of lymphogranuloma, an involvement of the small intestine, lower and mid ileum by a granulomatous infiltration having all the histologic characteristics of ileitis or of nonspecific granuloma Five lesions were found in the upper and more proximal part of the ileum the lowermost being six inches from the ileocecal valve The wall of the bowel was thickened, the lumen dilated, the mucosal surface was granular and showed numerous shallow ulcers

However from this exceptional case of lymphopathia venereum with involvement of the ileum, no conclusions can be drawn regarding ileitis as a virus disease at least not as the identical virus of the Nicolas Favre disease My own attempts at obtaining a positive Frei test in ileitis have been unsuccessful The frequency of recurrences in ileitis even after extensive resections and the inability to demonstrate a specific bacterial agency allows one to maintain an open mind on the possibility of a virus with a predilection for the ileal mucosa The fact that two observers did find involvement of the ileum in lymphopathia venereum suggests that a similar though not the identical virus may be considered as a possible true etiologic agency in ileitis

Allergy has been suggested by Tallroth as the etiologic agent, he described two case histories of "ileitis allergica" The finding of many eosinophils in the histologic sections was repeatedly stressed and obviously constitutes the basis for his suggestion The vascular injury was also typical of an allergic granulomatous process He regards the pathologic process in ileitis as a local anaphylactic reaction in the nature of an Arthus phenomenon

Sarcoidosis

The histologic pathology of Boeck's sarcoid and of ileitis is almost identical Homans and Hass stressed the similarity in the lymph gland pathology in the two diseases Longcope and Pierson in their thorough review of sarcoidosis make no reference to intestinal lesions Williams and Nickerson review 4 cases of sarcoidosis but without any ileal or intestinal or colonic involvement Snapper reviews the pathology, the clinical incidence and the histology of the two diseases terming them pseudo tuberculosis in nature He differentiates them sharply, however, in their respective clinical manifestations and considers them unrelated in all respects

More recently, isolated sarcoidosis of the small intestine simulating nonspecific ileo jejunitis has been described This is the first instance where the real differential diagnosis of ileitis from sarcoidosis involving the small bowel has been verifiably noted though in the literature small intestine involvement had been occasionally suspected In this paper by Watson and his associates two case histories are detailed which require analysis The radiographic picture resembled ileitis or ileo jejunitis Resected specimens had many of the characteristics similar to those of ileitis except for evidence of polyposis the histologic picture was almost identical *Hadfield in studying 20 cases of ileitis* had found 13 in which epitheloid cell tubercles were present and cautiously suggested the identity of ileitis and sarcoidosis

Moreland has just published an article entitled, "A Case of Sarcoidosis of the Lung with Regional Ileitis." A filling defect of the cecum was observed radiographically. At operation, resection of the terminal ileum was performed. Typical changes of a "sarcoid" nature were histologically observed in the removed mesenteric lymph nodes. This case is not convincing as one of ileitis. It could very well, however, be a good example of involvement of the ileum and colon in sarcoidosis.

The generalized picture of sarcoidosis in all its clinical manifestations, including skin and pulmonary lesions and the absence of fistulas, string sign and rectal complications have convinced most authors that the two diseases have little relationship. The most that can be said is that sarcoidosis may occasionally show involvement of the small bowel. Bernstein, Konzelman and Sidlick report a case of Boeck's sarcoid with true involvement of mucosa of the ileum marked by thickening of the wall with ulcerations measuring 2 x 4 cm. In the case of Lenartowicz and Rothfeld the gastrointestinal tract was diffusely involved. Homans and Hass stated that some observers have called ileitis "sarcoid of the small intestine."

TRAUMA

Mock (1931) in discussing infective granulomas states that "no case of granuloma the direct result of an accident such as from an automobile or a fall was ever reported." He makes an exception of course, for granulomata resulting from tears of the mesentery from direct violence to the abdomen, foreign bodies, splinters of wood, strangulated hernias and residual suture material. However, as early as 1936 Reichert and Mathes cite the case of a man who suffered a severe blow to the abdomen from the steering wheel of his automobile. Two weeks later he developed severe abdominal pain with vomiting and diarrhea. Late resection of the ileum revealed a granulomatous lesion twelve inches in length which was proximal to and not occupying the usual site for regional or terminal ileitis.

Two cases of regional enteritis following external trauma have been reported from the Mayo Clinic [176] In one case, three months prior, while the patient had been horse back riding, his mount had fallen on him delivering a severe crushing blow to the abdomen On exploratory operation some weeks later, an obstructing lesion was found about seven feet from the ileo cecal valve, relief followed a short circuiting procedure Later the lesion was resected

The second case involves a farmer who four months previously had been caught between two heavy farm implements, sustaining a severe crushing injury to the abdomen At operation, several loops of ileum were bound together by inflammatory adhesions and were fixed to one loop of lower jejunum which was definitely obstructed The usual edema of the mesentery and enlarged lymph nodes and *fistulous tracts so characteristic of ileitis were absent* These cases do not resemble ileitis in anatomic distribution or in symptomatology They represent true direct trauma to the small intestine with resultant granulomata and obstruction *Nominally they are instances of ileitis of traumatic origin*

ten Kate in 1936 very early reported two cases of regional enteritis following severe trauma In one case, a rupture of the ileum was found at operation, though nothing that resembled clinical ileitis In another case, a characteristic lesion with a fistula from the ileum to the bladder was observed at operation

Spellberg and Gray cite the case history of a soldier motor cyclist who ran into the end of a stalled truck Abdominal pain and vomiting supervened within thirty days X ray revealed a typical jejunitis beginning just below the fossa of Treitz At operation the jejunum resembled a garden hose being indurated and edematous, with accompanying enlarged lymph nodes Resection of the lesion was eventually required

In my own experience in spite of an initial skepticism, there seems to be sufficient basis for associating trauma and ileitis *in the relationship of cause and effect* (Crohn

[62, 63]) This conclusion is based upon experience with the following six cases briefly abstracted

Case 1 S I A man 39 year of age in an automobile accident was violently thrown forward against the steering wheel of his car sustaining ere abdominal trauma Abdominal cramp and diarrhea supervened almost immediately though the man had previously always been well Operation performed le than two weeks later because of the events of the complaints revealed a typical terminal ileitis cured by resection The patient received a large award from the courts This was my first experience of that type as an expert I testified against the likelihood of trauma creating such a lesion as ileitis though unable to deny the probable aggravation of a pre existent latent lesion My viewpoint was changed by the succeeding experiences

Case 2 J 4 A boy of 17 years of age always previously well was thrown violently across the aisle of a bus as it was involved in a collision striking his abdomen on the forward seat He immediately developed hematemesis and symptoms of a traumatic duodenal ulcer A gastroenterostomy was performed a few weeks later the stoma functioned badly At reoperation a typical regional ileitis was noted and resected It seems reasonable to deduce that both the duodenal ulcer and the ileitis which involved the terminal loops of the small bowel were traumatic in origin

Case 3 M M A 26 year old man suffered at 3 years of age a profound trauma when struck by a moving truck The child immediately developed an abscess in the right lower quadrant of the abdomen requiring several operations and characterized by an obstinate fecal fistula to the abdominal wall When 6 year of age the previously closed fistula reopened spontaneously and remained open for several months When 12 years of age the fistula again reopened but closed without surgical intervention The same sequence of events took place four years ago For the last ten months the patient has presented the typical symptom of regional enteritis with diarrhea fever and abdominal pain Two fecal fistulas present themselves on the anterior abdominal wall Radiographically the lower ileum is distorted in its mucous membrane pattern the mucosa of the terminal ileum is normal

Case 4 H 4 A woman of 50 lifted a heavy mat and immediately felt a pain in the right lower quadrant of the abdomen She suffered no diarrhea or fever Seven weeks later on physical examination a tender mass ege haped ma was noted in the right lower quadrant of the abdomen Radiographically a clear cut picture of ileitis was seen involving twelve to eighteen inches of the terminal ileum with several short fistulous tracts to the cecum and adjoining loops of small bowel The patient was observed for two years during which time successive x rays showed complete and spontaneous resolution The mass in the deep abdomen disappeared under observation

The lifting of the weight while not the cause of the ileitis was most probably a factor in bringing to light a latent and asymptomatic regional enteritis

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FAMILIAL INCIDENCE OF ILEITIS AS A POSSIBLE ETIOLOGIC FACTOR

Ulcerative colitis, nonspecific, a sister disease, rarely occurs in more than one member of a family. My own experience, and medical literature in general, bears out that fact. On the other hand, regional ileitis or enteritis occurs in multiple instances in intimately blood related members of a family sufficiently often to call for attention because herein may be a clue, if not to etiology, at least to familial predisposition. My notes on eleven such striking examples is of such interest as to warrant a closer analysis.

In 1934 the first instance of ileitis occurring in siblings was published. A boy of 14 (Crohn [58]) who represented historically a very early clinical history of ileitis was resected, and the diagnosis firmly established. Two years later, his sister many years older (32 years of age) complained of abdominal pain and vomiting and developed signs of intestinal obstruction. At operation a typical ileitis involving the terminal eight inches of small intestine was resected. The anatomic situation and pathologic attributes of the lesions were identical in both siblings.

In another pair of siblings, sister and brother, the same identical observations were made; in the sister the diagnosis being confirmed by operation. We have notes of two brothers both suffering with ileitis, one in the acute form slowly subsiding to spontaneous recovery, one going on to the chronic form requiring resection.

In two brothers, one had ileitis resected; the second brother was a case of typical ulcerative colitis. Mothers and daughters constitute a group which was seen three times, all the cases being confirmed. In one instance the mother had ileitis, the daughter ulcerative colitis. In a fourth instance the child had ileitis and the mother and two maternal aunts of the child had ulcerative colitis. We have

Case 5 M I A man of 2? years while in the Armed Service was severely stunned by the explosion of a bomb on board a U S destroyer Upon recovery he began to complain of abdominal pain and diarrhea The radiographic picture upon his discharge was typical of ileitis Interestingly he was able to continue in the Armed Services and obtained an honorable discharge Under observation the symptoms and radiographic evidence of ileitis has subsided and his case is considered one of spontaneous cure

Case 6 A man in an auto accident was thrown violently against the steering wheel of his car with severe bruises to his abdominal wall Two months after the injury he developed diarrhea abdominal pain and lost thirty pounds in one year A resection of the terminal ileum revealed a typical regional ileitis He was well after the operation for three years when he again suffered an accident this time being hit by a street car and thrown violently backward Immediately the diarrhea recurred A recurrence of the ileitis in the loop of ileum proximal to the previous anastomosis was suspected though not proven

Ileitis is a disease of great chronicity, often latent for years In the analysis of case histories in general it is not unusual to read of mild almost negligible occasional complaints for five, ten or twenty years, before the eventual diagnosis is established Nor is diarrhea a constant clinical symptom in ileitis or enteritis The thought seems therefore justifiable that in these instances where trauma has been related to ileitis actually one is dealing with an aggravation of a pre existing latent ileitis However the cases cited from the Mayo Clinic and the first three cases in my personal experience seemed sufficiently well checked and proven to allow the inference that the trauma preceded and caused the intestinal lesion In the other cases the aggravation of a lesion by the trauma seems justifiable

Traumatic enteritis in its clinical course is identical with ileitis as we know it in its well recognized forms Abdominal mass, fistula formation diarrhea fever are all present Segments other than those of the terminal ileum are more likely to be affected by the indiscriminate application of the trauma

Spontaneous resolution was twice observed an incidence that would seem higher than in the control nontraumatic cases

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again noted an uncle suffering with ileitis, his niece with segmental or right sided colitis

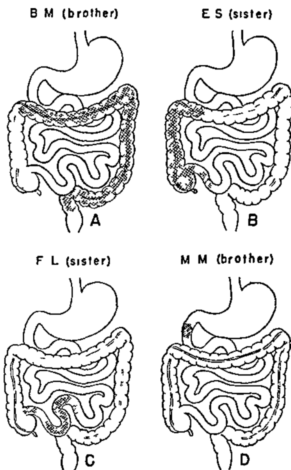


Fig 1—Familial Incidence in Four Siblings (A) Ulcerative colitis (B) segmental colitis (right sided) (C) regional ileitis (D) duodenal ulcer

Further, three family groups afford a striking picture In the first, a young woman her brother and her half brother, have ileitis the father is suffering from ulcerative colitis In the second family group we note ileitis, seg

mental colitis, and ulcerative colitis in three adult siblings (fig 1) In the third family group a child and her two aunts by consanguinity, have all had ileitis confirmed by operation Bockus refers to two cousins suffering with regional ileitis with extension into the colon, ileocolitis both resected and well They had previously lived *together* in the same house Brown and Scheflly have reported regional enteritis affecting three siblings, two sisters and one brother *In two of the siblings the colon was involved* as well as the terminal ileum Very recently a case of regional ileitis in a father *and* son has also been described [135]

The significance of these findings remains conjectural they are too interesting, however, to be dismissed without consideration *If a proven bacterial or viral agency* could be incriminated as the cause of ileitis or of ulcerative colitis one could understand contact infection, such as occurs in epidemics of bacillary dysentery or in amoebiasis, by finger transmission or by insects particularly flies Or one could conceive of a common vector Since such a specific etiologic agent is not known, it seems more logical to fall back upon at least a familial predisposition to the unrecognized infective agency such a *factor* predisposing to ileitis to ulcerative colitis or to both diseases The mixed cases of ileocolitis seen in this series only again draw attention to the common liability *of* small and large intestine to the offending agency

THEORIES REGARDING THE PATHOLOGIC MECHANISM IN THE CREATION OF ILEITIS

Most of the hypothetic considerations regarding the actual location of the lesion, and the possible direct physical factors in initiating the granuloma have *centered* about the terminal ileum and the ileo cecal valve This viewpoint disregards *the* fact that the lesion may *occur* at any level of the small intestine and also that recurrences of ileitis

occur far from the original site of inflammation and from the valve of Bauhin

Naturally the first suspicion was directed at the appendix as a causative factor. Many writers have suggested that a fibrinoplastic process beginning in the appendix extended to the ileum, thus constituting terminal ileitis (Lowen). Fischer made the same claim but this time through the mediation of the mesenteric lymph nodes. Ravdin and Rhoads again pointed out the similar pathologic changes in fibroplastic appendicitis, and the chronic stage of regional ileitis. Homans and Hass, and Erb and Farmer, suggested primary appendiceal disease as an etiologic factor.

In refutation of this idea, it should be noted that the appendix had previously been removed in over 25 per cent of cases of ileitis. The life course of the disease is in no way *altered or stayed*. *The resected appendix, apart from* showing slight chronic changes of the usual type seen in adult life, is free of typical granulomatous changes such as characterize granulomata and ileitis. I know of only two cases where acute phlegmonous appendicitis occurred some years subsequent to a short circuiting operation for ileitis. Nor is there reason to expect the appendix to be involved in ileitis since the appendix originates from the base of the cecum, beyond the ileo-cecal valve and is separated anatomically from the ileum by the ileo-cecal valve, which is such an efficient barrier in preventing the spread of the ileitis to the cecum. Nor does acute appendicitis occur more frequently in the combined cases with cecal involvement. *Histologically the appendix in the resected* specimens of combined ileo-colitis does not participate in the peculiar and characteristic granulomatous inflammation.

VASCULAR CHANGES

The analogy of ileitis with intestinal granulomata might well suggest that the similar pathologic picture in both diseases result from an identical impairment of the blood supply. Those authors who have written on the subject of

granulomata of the intestinal tract have emphasized volvulus, intussusception, strangulated hernia, and traumatic rents as direct causative agents leading to granulomatous mass formations Ginzburg and Oppenheimer particularly stress the reduced vascularization that results in mucosal necrosis ulceration and secondary hyperplastic granulomatous changes Barbour and Stokes mentioned the possibility of a chronic recurrent intussusception Bockus and Lee discussed the peculiar blood supply of the terminal ileum and its mesentery, suggesting that the terminal branch of the ileo colic artery might be compromised by undergoing rotation Bell, however, in experimental studies could not reproduce granulomata by interference with the blood supply

THE THEORY OF LYMPHATIC BLOCK

Of much greater interest is the question of the relationship of the mesenteric lymph glands and the lymphatics of the intestinal wall to granulomatous ileitis The constant finding of enlarged lymph nodes in the mesentery of the affected loops of intestine, while easily explained on the basis of secondary infection, has caused some writers to advance the hypothesis that the primary lesion may be resident in the lymphatic tissues, the organic changes in the wall of the gut being secondary thereto Holman, in discussing a paper by Bell in 1934, asks whether the lymphatic hyperplasia is an expression of a chronic infection originating in the bowel or is it possibly the primary lesion with subsequent fibrosis and secondary constriction of the intestinal canal? Two years later, Reichert and Mathes published a paper on 'Experimental Lymphedema of the Intestinal Tract and its Relation to Regional Cicatrizing Enteritis The dominant features of the intestinal lesion in ileitis resembled a low grade infection with a concomitant chronic lymphatic obstruction and edema They observed the pathologic resemblance to elephantiasis as seen in the extremities of the body In animal experiments, using a fine needle, sclerosing substances were injected into the

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teral absorption Studies on the ileo cecal junction (ileo cecus) by Bargen and his associates demonstrated longitudinal muscle fibers entering the labia of the valve for a considerable distance and meeting at the crest Gelatin solutions injected at the cecal mucosa were blocked at the tip of the labia, similar injections made on the ileal side in 15 cadavers were also blocked at the valve Obviously there is a lymphatic blockage at the tip of the labia of the ileo cecal junction

The possible relationship of acute mesenteric lymphadenitis to acute and chronic regional enteritis presents an interesting thought Jackson suggested the kinship of the two diseases However, in 15 cases he found only a mild hyperemia of the terminal 3 to 4 inches of the terminal ileum, he has no record of any case of ileitis originating in, or from acute mesenteric lymphadenitis Rockey noted thickening of the ileum in children with acute mesenteric lymphadenitis in 4 cases All were valid cases of acute ileitis with marked lymph adenopathy, and this in September 1932 before the first publication on ileitis

On the other hand, Eliason and Johnson state that they know of no case of acute ileitis originating in acute mesenteric lymphadenitis In the 15 cases of acute ileitis observed by them, and operated upon, they found *no* intraperitoneal picture that resembled acute mesenteric lymphadenitis either as regards abundant free peritoneal fluid, or massive disseminated lymph gland enlargement

In 1932 Strombeck published his observations on 40 cases of acute nontuberculous mesenteric lymphadenitis controlled by operation In 22 instances, he noted the occurrence of acute terminal ileitis which he presumes was the point of origin of the infection Ten to 20 to 50 cm of terminal ileum proximal to the ileo cecal valve were involved, the intensity of the affection being at the valve and diminishing upward The Peyer s patches were large and " grainy boat shaped swellings " The greatest frequency occurred between the ages of 5 and 15 years corresponding to the

mesenteric lymphatics and serosal lymphatics of the wall of the intestine

The materials used for sclerosing purposes included crystalline silica mesh, bismuth oxychloride, indelible lead or sodium morrhuate In some animals, a 24 hour broth culture of B coli was given intravenously one to three hours before the lymphatic injection, those bacterial injections occasionally being repeated at intervals subsequent to the acute experiment When the animal was sacrificed, the treated segment of bowel felt thickened, some of the mesenteric lymphatics were dilated, some sclerosed Free peritoneal fluid was not present The thickened bowel wall showed inflammation and thickening of the serosa, edema of the circular and longitudinal muscle fibers, the submucosa was swollen and infiltrated with leukocytes, the mucosa swollen but not ulcerated Chronic pathologic changes persisted without subsidence for months after even a single sclerosing injection The changes were seen in all specimens (12) examined, but were most marked in those experiments *in which bacterial suspensions were intravenously injected coincidentally with the lymphatic block The intestinal lymphedema was found to persist as long as ten months without any evidence of subsidence*

It is interesting to note that Poppe, using similar method of lymphatic sclerosing injections, claims to have produced ulcerative colitis in dogs by obliteration of intestinal lymphatics However, Sinaiko and Necheles, repeating their work, not only failed to produce ulcerating lesions in the colon of dogs, but point out, in contradistinction to the results of Reichert and Mathes that the lesion in the colon showed a tendency to rapid disappearance and no tendency to chronicity

It had already been suggested (Probstein and Gruenfeld) that normally the flow of the intestinal content is retarded at the ileo cecal valve, the lymphatic tissue in the mucosa and submucosa is here more *abundant than in the segments of the bowel, a factor which enhances the likelihood of bac*

is well represented Childhood and old age are scantily represented The oldest case was 71 years at observation the youngest case was 9 months in one instance, and 2½ years in another instance The 9 months old case was confirmed by operation and by x ray studies

These figures agree well with those of other authors who have collected large series of cases Thus Strombeck collected from the literature 91 cases, the greatest incidence (40 cases) fell between 20–30 years of age, namely 44 per cent, agreeing almost identically with the figures in this series Similarly, Ravdin and Johnston in a collection of 393 cases from the literature give the age incidence as shown in table 2

TABLE —*Age Incidence in Regional Ileitis (Ravdin and Johnston)*

Age Group	*Number of Cases*	*Percentage*
1–10	18	4 7
10–20	68	17 8
20–30	140	36 6
30–40	76	19 9
40–50	40	10 4
50–60	4	6
60–70	13	3 4
70–80	3	0 8
Total	38	

Sex

Males predominate over females in their susceptibility to this disease In this present series, there were 124 males and 98 females involved representing a proportion of 56 per cent males to 44 per cent females These figures again agree with the mass compilation of cases from the literature in which males constituted 56 6 per cent of the cases (Ravdin and Johnston) The figure given in earlier years based on a smaller group of cases (Crohn [59]) of males predominating over females in a proportion of 2 1 is not borne out when large group statistics are invoked

Schiff garnered the statistics from the literature on 48 cases of ileitis in childhood The ages varied from 1½ years to 16 years as shown in table 3

greatest frequency of acute ileitis Strombeck distinctly states that in the follow up covering at least four years, he has never seen any such case develop into the picture of a chronic regional ileitis Of 31 cases of nontuberculous mesenteric lymphadenitis observed by Erskine 10 showed some involvement of the ileum in an inflammatory process associated with large hypertrophied lymph nodes in the mesentery He does not relate the disease to true regional ileitis In his opinion the lymph nodes are first involved and then the appendix or the ileum or both by an extension of the process

The observations of Strombeck more or less dispose of the hypothesis that chronic regional enteritis begins as an acute mesenteric lymphadenitis The largest percentage of cases of ileitis in this series (222 out of 238 cases) were chronic in nature throughout their course The abdominal findings at operation in acute mesenteric lymphadenitis is generalized enlargement of mesenteric lymph nodes, much clear fluid, occasional involvement of terminal ileum In acute ileitis, one observes scant free fluid, edematous engorgement of the terminal ileum and only localized lymph node involvement Perforation of the acutely inflamed ileum with localized walled off peritonitis is not unusual

Age in Regional Ileitis

In our series the age distribution at onset of symptoms may be noted in table 1

Table 1—*Age Distribution at Onset of Regional Ileitis*

Years	*Number of Cases*	*Incidence (%)*
1–10	6	2.7
10–20	54	24.4
20–30	98	44.2
30–40	49	22.0
40–50	9	4.0
50–60	4	1.4
60–70		0
Total	222	

The average age at onset was 27.8 years The maximum incidence falls between 20–30 years, though adolescence

both psychic strain and physical disease as the background for the etiology of regional ileitis is seen in the following case

H B Serial No 20 male age 29 years Patient enlisted in the U S Army in 1939 serving in the Philippine Islands He was a prisoner of war to the Japanese from 1942 to 1945 one of the many who participated in the Death March from Corregidor He suffered from *bacillary dysentery amebic dysentery, undulant fever malaria* pellagra scurvy beri beri and severe malnutrition During all this time he had severe diarrhea In July 1945 the diagnosis of regional ileitis was made by x ray examination the granulomatous process involving the whole of the ileum When seen in 1946 he had recovered weight and strength and was well except for the diarrhea X ray examination demonstrated a normal colon but a severe diffuse regional ileitis The sigmoidoscopy was negative (fig 2)



Fig 2—Regional Ileitis in a Man who Survived the Death March and Three Years in a Japanese Prisoners Concentration Camp Favorable clinical course under medical therapy

All classes of society are affected equally by ileitis, private hospitals and public wards seem equally represented

TABLE 3—*Age Incidence of Ileitis in Childhood (Schiff)*

Age	*Number of Cases*
1¼ years	1 case
2–3 years	4 cases
4–6 years	6 cases
7–9 years	18 cases
10–12 years	5 cases
13–14 years	7 cases
15–16 years	7 cases
Total	48 cases

He emphasized particularly the acute phase of the disease in children and the similarity of the clinical picture to that of acute mesenteric lymphadenitis

SOCIAL STATUS, RACE, RELIGION, NATIONALITY

It is unlikely that any of these social factors play a role in the etiologic incidence of the disease Bockus says of the personal pattern that very few of these cases are phlegmatic and calm, they are usually sensitive, emotional and excitable Four of 19 cases in his series were severely psychoneurotic, in 2 of them the disease having been treated as a neurosis My own observations do not impress me with the fact that the ileitis case is much different than a control group of the population True, many of them are high strung and anxious, in several instances the patients had been institutionalized for psychoneurosis or anxiety state, the diarrhea having been completely overlooked The secondary nervous manifestations resulting from prolonged illness, diarrhea, inanition loss of weight and anemia may simulate a psychoneurosis but only to the uninitiated (Blackburn)

The personality of the ileitis case is more stable than that of the patient suffering from ulcerative colitis or of peptic ulcer He has less of the psychosomatic factors so evident in both these latter groups However, the number of cases of ileitis *that have been rescued from institutions for the* treatment of mental diseases emphasizes not the personality but the end results of the drain of the disease upon the psychic constitution of the sufferer An interesting instance of

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in proportion to population. Bockus seems impressed with the failure to encounter regional ileitis in families who have been in the upper economic brackets for one or two generations. All races and climes seem represented in this disease since the literature from all over the world contains publications of cases (Africa, India, Sweden, Puerto Rico [8], East Africa [130], South America [26–28]). Bockus again mentions the fact that no cases had been reported from Latin America or from Cuba. This deficiency has since been supplied in an article based on experiences in Puerto Rico. He also observed paucity of cases from the southern sections of South America. In 1944, there were 134 admissions from ileitis in the total U. S. Army; in 1945 there were 145 similar admissions for the entire Army. The corresponding rate per 1000 strength for each year is .02 (personal communication). Kiefer found that regional ileitis occurred seventy times in 100,000 registrants at the Lahey Clinic.

As regards race, a greater incidence of the disease among the Jewish race was first suggested by Homans and Hass. In the series by Mixter, 8 of his 11 patients were of Jewish origin. But as these patients were reported from the Beth Israel Hospital at Boston as were mine from the Mount Sinai Hospital in New York, both being institutions with predominant Jewish admissions, this race incidence was not particularly noteworthy. In the experience of Bockus, 13 of 21 cases were Jewish, thrice the normal expectancy of the disease for the sample from which the cases were drawn. However, in Marshall's series, at the Lahey Clinic, only 3 of 29 instances were Jews. Ashley at the Harper Hospital in Detroit found only 8 of 31 cases in his series to be Jews, Brown and Donald 26 per cent Jews (Mayo Clinic). The study comprising 22 cases of ileitis in the records of the Binghamton City Hospital and other hospitals in Broome County, New York State, include no cases involving Jewish patients (Sneirson and Ryan). Negroes, Orientals, Latin Americans are all represented and reported in the literature; one of my own cases was a

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Gross Pathology

REGIONAL ILEITIS is a nonspecific granulomatous inflammation of the ileum, involving most frequently the terminal segment or segments of the small bowel In gross appearance it has definitely characteristics that distinguish it from granulomata elsewhere in the alimentary tract, these specific features being most pathognomonic when the terminal ileum alone is involved The histologic microscopy of the disease is nonspecific and not to be differentiated from other granulomata, from sarcoid and often only with difficulty from tuberculosis

In our series of 222 cases, the extent of ileal invasion was noted in our records in 156 instances The inability to state the amount of anatomic involvement in the remaining cases was due to the fact that they had been previously operated elsewhere or that no surgical corroboration of the radiographic picture had been obtained

The anatomic distribution in this series may be seen in table 4

TABLE 4 — *Anatomic Distribution in Regional Ileitis (Fig 3)*

Distal (inches)	*Cases*	
4	8	
6	18	Terminal 12
8	16	inches 83 cases
10	14	
12	[illegible]	
15	17	Terminal 24
18	15	inches 47 cases
24	15	
30	8	Extension to
36	8	the remainder
48	3	of ileum 6 cases
60	4	
84	3	
Total	156	

In one remaining case, the terminal ileum and the uppermost ileum were discontinuously involved The predominance of the lesion limited to the terminal 12 inches of ileum is noteworthy, the next longest group involves not only the terminal segment but extends continuously to cover the distal 24 inches of ileum, the smallest group involves the terminal and all of the upper reaches of the ileum which we arbitrarily indicate as being about seven feet

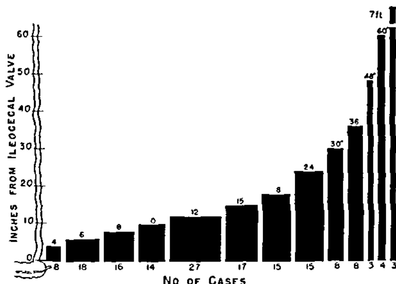


Fig 3—Regional Ileitis Anatomic Distribution of Pathologic Lesion (156 Cases) Table represents area from ileo-cecal valve to general region of transition from ileum to jejunum Majority of cases fall between 8 and 15 inches from the ileo-cecal valve

in length from the ileo cecal valve In the series of cases reported by Blackburn, Hadfield and Hunt, of 23 cases the terminal ileum was involved in 19 instances the distal ileum in 3 instances In 6 cases the cecum was involved in an analogous extension of the process The length of ileum involved varied between 4 and 60 cm with an average of 19 cm (7½ inches)

Why the terminal ileum is so often the sole seat of the disease and apparently the oldest and parent lesion in

the process is difficult to state. Most diseases of the small bowel are located at or near the terminal ileum just proximal to the ileo-cecal valve. These include benign and malignant new *growths, foreign body granulomata, primary* and secondary hyperplastic tuberculosis, sarcoid, carcinoid and endometriosis. The normal narrowing of the lumen of the small bowel as it progresses distally is maximum just proximal to the valve of Bauhin, the valve itself constitutes a mechanical device for *slowing up the progress* of the column of chyme, the lymphatics of the intestinal wall, particularly the mesenteric lymph nodes are in their greatest density at or about the ileo-cecal angle. The natural blockage of the lymphatic drainage at the labia of the valves, as shown by Bargen et al, localizes an infection proximal to the valve and discourages or prevents in the largest percentage of cases, the transition or extension of the disease to the cecum. Occasional cases are cited where the lesion involves a small segment of ileum proximal to the valve without involving the actual terminal segment of the ileum, but these cases are exceedingly rare.

The gross appearance of ileitis as seen at the operating *table or as studied in the resected specimen is that of* a brilliantly red congested edematous mass, solid and firm, resembling a rubber hose, or as Dalziel has described it, of "an eel in a state of rigor mortis." An equally apt description is that of Jackson who likened the diseased segment of ileum to "a dead water-soaked night crawler." The serosal surface is greatly injected, usually covered by a fibrinous exudate, the lumen of the gut may be dilated, *or in the end stages reduced to a narrowed cordlike tube.* The extent of involvement is manifest by the varying degrees of hyperemia, the engorgement of the vessels, the serosal exudate and by the gross enlargement of the accompanying mesenteric lymph nodes. The hyperplasia of the mesenteric lymph nodes parallels the extent and degree of the inflammatory lesion. Where the lesion ends, usually more or less abruptly, the serosa of the proximal bowel

appears normally shiny and smooth, and the obviously enlarged mesenteric nodes are no longer visible

The mesentery of the involved bowel is boggy, swollen and visibly thickened. Usually one or more loops of small intestine are matted together forming a palpable inflammatory mass. On attempting to separate the loops it will frequently be noted that they are adherent because of fistulous communications, fistulous tracts originating

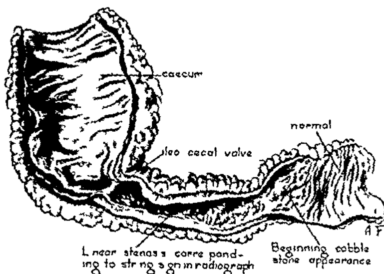


Fig. 4—Characteristic Lesion in Typical Terminal Ileitis (Regional) Note the diminished lumen which is the basis for the string sign

in the terminal ileum extending through the mesentery to the adjoining loops of small or of large bowel. Occasionally a slow walled off perforation of the terminal loop of ileum will be observed covered over by a plastic exudate and sealed off by neighboring viscera usually another loop of ileum or the sigmoid. Bockus emphasizes the point that there is a close relationship between the destructive changes in the mucosa and the extent of covering of the serosa with mesenteric fat. The termination of the mesenteric fat

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lumen of the bowel itself is reduced and compromised by the swelling of the walls until the actual lumen is reduced to a cord like stenotic opening. This reduction of the lumen of the bowel in old chronic distal ileitis accounts for the characteristic "string sign" as seen in radiographic films. The process may continue to true stenosis with intestinal obstruction and proximal dilatation of the bowel loops, the stenosis being due to cicatricial contraction of old inflammatory scar tissue at the site of the ulcerating lesions.

The mucous membrane has a cobble stone appearance due to the fact that the transverse folds of the mucosa are in part destroyed and are intersected by deeply grooved longitudinal ulcerations that extend through the length of the specimen. These longitudinal ulcerations are deepest along the mesenteric border or attachment; it is in this area along the mesentery that the sinus and fistula tracts emanate. The surface of the mucosa is superficially desquamated, the markings are gone; deep ulcers 0.5 cm. to 1 cm. in diameter are interspersed between areas of proliferated almost polypoid hyperplastic mucosa. True polypoid formation in late cases, as is seen in ulcerative colitis, is rarely observed. The submucosa is markedly thickened and edematous and congested; the muscularis is thickened and hyperplastic; the serosa, its sheen gone, is bright red, many times its normal thickness in depth and covered by exudate.

The gross lesion in the bowel wall terminates rather abruptly; a sharp line of demarcation is lacking, but the mucosa within one or two inches of the proximal area of involvement will suddenly lose its edema and thickening and shortly resolve into normal mucosa. Unfortunately the *inflammatory process has a tendency to extend proximately* by kangaroo like jumps; "skip lesions" of involvement are common proximal to the distal involved segment, these "skip lesions" being separated by "skip areas" of normal

on the antimesenteric portion of the serosa corresponds to the line of demarcation between diseased and normal mucosa

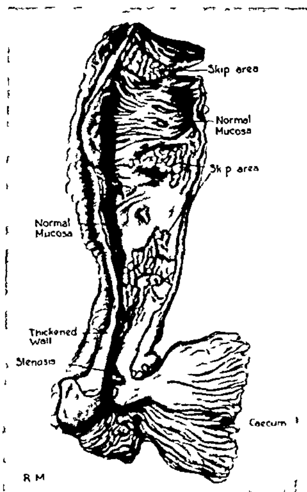


Fig 5 — Characteristic Arrangement of Lesion in Terminal Ileitis The most terminal segment of the ileum proximal to the ileo-cecal valve shows the characteristic stenosis of the lumen as the basis for the formation of the string sign

Upon opening the resected specimen one notes the edema and thickening of all the coats of the bowel (figs 4, 5) The

stitutes to a large degree the disappointing end results of surgical intervention

Microscopic Pathology

There are no specific features that characterize or are pathognomonic of ileitis in contrast to granulomata or so called pseudo tuberculous diseases in general The stained sections show varying degress of acute subacute and chronic inflammation, predominantly marked by infiltration of polymorphonuclear leukocytes, plasma and round cells and fibroplastic elements The earliest lesion is apparent in the submucosa where the intensity of the lesion is the greatest (Hadfield), (Schepers) The mucosa is desquamated the architectural structure of the glandular tissue is destroyed and replaced by plasma and round cell infiltration In the late stages of the disease the inflammatory reaction is more focal in character covered on the mucosal side by nodular thickening reminiscent of tubercles The enlarged congested skeins of inflamed lymphatics are often apparent even through the thickened serous peritoneal covering

Microscopically the presence of giant cells is very striking In the vicinity of the giant cells one often sees groups of pale cellular structures resembling vegetable cells in nature The giant cells are not specific to ileitis they had been noticed previously by Moschcowitz and Wilensky in their study of intestinal granulomas and were thought by them, and by subsequent writers, to be due to foreign body inclusions vegetable matter or lycopodium spores Homans and Hass thought the giant cells to be a reaction to lipoid material Reichert and Mathes to possible silica or talc inclusions This vegetable material becomes entrapped in the deep mucosal ulcerations, enters the lymphatics and becomes encapsulated in the process of healing The attempts of earlier authors to include ileitis as a form of tuberculosis was probably due to the findings of giant cells of the Langerhans type

mucosa. The extent of the skip may vary from a few inches, or in multiple "skip lesions" to several inches, up to 2½ feet between the parent and the "skip lesion" (fig. 6).

In older phases of the disease, the exudative or inflammatory reaction is replaced by a fibrostenotic process, the mucosa appears atrophic with occasional superficial erosions and islands of papillary or polypoid hyperplasia. The lumen of the gut may be so reduced as barely to admit a large probe.

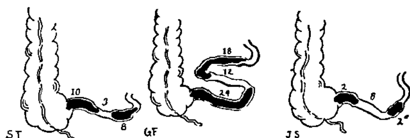


Fig. 6.—Varieties of Skip Lesions and Skipped Areas in Ileitis. Figures represent inches.

Pemberton and Brown have made an important contribution in differentiating the lesion in ileitis into two categories: (1) Involvement of a shorter or localized segment of the ileum, a single lesion. (2) a similar process which involves larger segments, usually multiple with a greater tendency to progressive extension. Clinically, this differentiation on a pathologic basis seems amply verifiable. The first or localized group may and does progress to stenotic fibrosis, remains stationary and may lead to intestinal obstruction. They lend themselves favorably to surgery. *The second group is scattered progressive*, in the nature of a mucosal or submucosal lesion less well defined anatomically with less involvement of regional lymph nodes, and less amenable to accurate definition during exploratory operation. This, the "mucosal" or submucosal type con

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Fig 7 —Pseudo tubercle with Epithelioid Cells Arranged in a Whorl around Giant Cell in Submucosa (Regional Ileitis)

Fig 8 —Lymph Node Showing Pseudo tubercle Formation with Giant Cell Systems

Hadfield has made an intensive histologic study of twenty resected specimens at St Bartholomew's Hospital in London He particularly emphasized the early and intense involvement of the submucosa considering that the mucosa was probably secondarily involved in the process by extension and by necrosis due to vascular infiltration The changes early in the submucosa consist of hyperplasia of the lymphatic tissue and obstructive lymphedema The submucosal

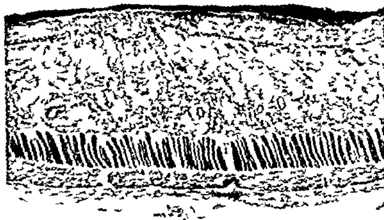


Fig 9—Longitudinal Section of Skip Lesion in Regional Ileitis Showing Marked Submucosal Thickening due to Granulomatous infiltration Epithelium completely ulcerated and surface covered with a purulent exudate

hyperplasia and early and extensive involvement of the lymphatics occurs in his experience in 95 per cent of the cases These early areas of lymphadenoid tissue show clear evidence of cellular activity with a central zone of proliferating reticulum cells surrounded by a narrow zone of lymphocytes (figs 7 and 8) A specific response occurs The affected germinal centers become replaced by proliferat

ing endothelial cells A Langerhans giant cell can usually be found at the center of the nodule The follicle now becomes a "giant cell system" Hadfield states that in the several *hundred sections he has examined* caseation has never been observed The typical specific reaction, with giant cell inclusions, characterized the sections of lymph nodes found in the mesentery and accompanying the specific lesion in



Fig 10—Cross Section of Chronic Terminal Ileitis Showing Stenosis of the Lumen Caused by Extensive Granulomatous Infiltration of Submucosa

the gut (figs 9 and 10) Actually, Hadfield found giant cells in 13 out of 20 cases examined Necrosis within the granulomatous areas in the ileum or in the lymph nodes rarely occurs caseation never In the series of Warren and Sommers, necrosis was observed in *8 of 61 cases (13 per* cent) Reference has been made to the case of Frazer and Haggar in which caseating tuberculous mesenteric lymph nodes were observed in the resected specimen though the ileitis proper *was nonspecific in origin*

Endarteritis obliterans and perivascular infiltration with collections of plasma cells were emphasized by Binney. Early involvement of nerve tissue particularly Auerbach's plexus was noted by Barbour and Stokes, though these changes are not specific. They even suggested that a chronic recurring intussusception might initiate the process by impairing the circulation and vitality of the gut wall. Schepers divides the lesion into two components: a primary phase characterized by (a) a stage of edema of the submucosa and the serosa with dilatation of submucosal lymphatics and hyperemia of juxtamuscular adventitial blood vessels, (b) plasma cell infiltration of submucosa and serosa, (c) diffuse fibrosis with disappearance of plasma cells, (d) healing; a secondary phase characterized by ulceration of the mucosa and submucosa which is superimposed on the primary phase with eventual tendencies to late or early perforation, fistulation and granuloma formation.

4 Clinical Features

Onset

THE USUAL CASE of regional ileitis begins not as an acute and sudden manifestation, its onset is usually hidden in the deep past, with such intervening symptoms as an occasional spell of diarrhea, a progressive malaise, or as nervousness often verging on true psychoneurosis. A rectal suppurative complication may long precede the manifest initiations of diarrhea. Gradually the diarrhea increases in severity and is now accompanied by abdominal pain, occasionally low grade temperature is noted with loss of weight. In the prodromal stages the patient loses little efficiency or time from his work or occupation. The progressive symptoms build up over the course of years to the finally fully developed picture of regional ileitis. Such is the most common picture of the onset. Some unusual forms of onset have been noted in this series such as initial intestinal obstruction, 2 cases; onset with hematemesis and melaena, 2 cases; onset with dysuria, one case; onset with sealed off perforation, one case.

The duration of symptoms before the actual recognition and diagnosis of the disease, in this series may be seen in table 5.

TABLE 5.—*Duration of Symptoms before Recognition of Regional Ileitis*

0–3 months	8 cases
3–6 months	14 cases
6–12 months	15 cases
1–3 years	50 cases
3–5 years	[illegible] cases
5–10 years	33 cases
10–20 years	6 cases
50 years	1 case
Total	183 cases

It will be seen that the largest group of cases falls between one and five years as the duration of the symptoms before the initiation of therapy the next largest group falls between five and twenty years before recognition of the disease The one with a fifty year unrecognized diagnosis was a Hindu from British India Blackburn states that the average duration of symptoms before operation was 31½ months Clark and Dixon found that the average duration of symptoms before coming under observation was 4 1 years, the longest duration of symptoms was 25 years

If one were to speak of prodroma one could mention only the suppurative rectal complications which so often precede by years the onset of manifest symptoms These rectal or peri rectal abscesses and fistulas occurred in 44 of the 222 cases the real significances lies in the fact that they so often precede the onset of diarrhea If they do not actually antedate the diarrhea, they are so obvious and the diarrhea so minimal that to most uninitiated observers only the fistula or peri rectal abscess exists On one occasion a patient who was admitted to the wards for routine hemorrhoidectomy was observed to have a small rectal fistula An alert resident physician detected a vague history of diarrhea, and asked for radiographic study which disclosed a terminal ileitis

The one other phenomenon which stigmatizes the onset of ileitis is the scar of a previous appendectomy This scar was evident in 68 or 30 6 per cent, of our series of cases and was a signal of previous abdominal pain localized in the lower right quadrant of the abdomen Ravdin and Johnston found in a review of currently published cases in the literature that a previous appendectomy had been performed in 27 1 per cent of the cases The diarrhea which characterizes most of the cases of ileitis was undoubtedly overlooked the abdomen was opened, an innocent appendix removed and the ileitis not observed

The onset of the true symptoms of ileitis or enteritis

is characterized, when typical, by the initiation of diarrhea, abdominal pain, low grade fever progressive anemia and loss of weight and eventually by the ability of the clinician to feel an intra abdominal mass *Diarrhea* was present in 165 of the 222 cases of regional ileitis The diarrhea is an outstanding feature of the disease, though in number of movements and in intensity it rarely approaches that of ulcerative colitis The rule that "frequency of fecal movements in an inflammatory intestinal process is in inverse proportion to the distance from the anal sphincter," holds good Ulcerative proctitis gives usually 10 to 20 stools a day with urgency, tenesmus and the appearance of fresh blood in the stools Ulcerative colitis in the distal colon may average 5–10 stools a day, right sided or segmental colitis is notable for lessened frequency of defecation, perhaps 3–6 per day Regional ileitis with all its pathologic process proximal to the ileo cecal valve is noted for milder diarrhea, 2 to 4 or 5 movements in twenty four hours

Each individual movement is usually preceded by a spasm of abdominal pain The characteristic sequence of events is similar to the classic description of Moynihan regarding duodenal ulcer, where it is "pain food, relief, pain" In ileitis, the sequence is abdominal pain or colic, desire to defecate, the feeling of sudden rumbling of gas, followed by defecation with relief of all subjective abdominal symptoms, so called predefecation pain This sequence may repeat itself every few hours of the day less at night, it is often initiated by the taking of a meal The defecations are not urgent are not spurting in nature The stool is mushy, semi formed or liquid contains some excess of fluid mucus never evident pus and rarely blood (11 instances out of 222) In fact occult bleeding in the stool on examination with guaiac is usually negative Hurst, however, reports 5 cases of regional ileitis and 2 additional cases previously noted in all of which occult blood was regularly found in the stool The stool may be slightly acid or alka

line or it may be neutral the reaction here has no significance

Either a normal number of daily movements (41 cases) or constipation (18 cases) mark the remainder of the cases in this series Not infrequently even in a mature case of ileitis no history of diarrhea is obtainable and in some few cases (18 in all) actual constipation was noted The presence of constipation does not necessarily denote obstruction since only in the late phases of intestinal obstruction is the constipation acute and obdurate In those cases in which constipation has been present, the remaining symptoms of abdominal pain colic, a mass and a progressive course have also been negligible, the radiographic study establishes the diagnosis

Abdominal pain was noted in 126 instances in this series This figure is surprising for pain in the abdomen seems so constant a complaint in the anamnesis that one would expect its presence in a much higher percentage of the cases The pain is usually mildly colicky in nature, most often situated in the lower abdomen, preferring the right lower quadrant or the suprapubic region in its site Occasionally the pain is solely in the left lower quadrant and in a few cases covers the whole lower and upper abdominal segments The pain precedes and is relieved by defecation When the inflammatory mass becomes adherent to the sigmoid loop of colon and pinned down to that viscus by internal fistulas the pain and the mass is likely to be localized in the left lower rather than the right lower quadrant of the abdomen

The origin of the pain is in the mildly obstructive narrowed loop of the ileum that segment which radiographically corresponds to the 'string sign The attempt of the intestinal fluid column to pass through this congested, edematous and narrowed stretch of intestinal lumen gives rise to the colicky sensation of pain The absence of pain occurs in those cases in which the inflammatory lesion is diffuse the 'mucosal type in which the beginning ulcer

trical process is still young, the mucosal pattern is altered by the stenosing string sign, the quill like narrowing has *not yet supervened* *The higher the process in the ileum, the* less likely the stenosis and hence the less likely predefecatory pain In the late *long standing* cases where true stenosis supervenes, the pain is of course severe and sharply colicky Occasionally primary intestinal obstruction characterizes the onset of regional ileitis, or at least its symptomatic phase Such was the unusual onset in the case quoted by Dickinson and Zimmerman

Nausea and vomiting are rare manifestations and occur only in the later stenotic phase of the disease Appetite is usually well preserved, this is in contrast to ulcerative colitis, where loss of appetite, absolute anorexia and even vomiting are common manifestations and parallel the intensity of the toxic process Ulcerative colitis is a much more "toxic" disease than regional ileitis and the interference with appetite and with nourishment is in contrast to the *milder manifestations and retained desire for food* which is present in ileitis

Fever occurred in 69 cases of the 222 cases in this series The fever is of the low grade type, the temperature usually normal in the *morning*, rises to *100 5*, *101* or rarely *102 F* in the late afternoon It is irregular in type, though often persisting, it is not accompanied by chills or sweats Many, if not most of the cases are afebrile throughout The fever characterizes the acute or inflammatory phases of the process, the intervening stages of remission are afebrile, the late cicatrizing phase of the disease is again afebrile

The continuous low grade fever of ileitis like that of segmental or right sided colitis is frequently mistaken, where the diarrhea is minimal and unnoticed, for many of *the other diseases which are also characterized by low* grade fever and low leukocyte counts in the circulating blood Undulant fever brucellosis subacute bacterial endocarditis, lupus erythematosis disseminatus are frequently the connotations given to the low grade febrile type of

ileitis without any noticeable diarrhea or abdominal pain

The leukocyte count in the circulating blood in ileitis is not usually materially elevated The range may be between 9,000 and 12 000 white blood cells, rarely higher A shift to the left of the polymorphonuclear leukocytes and toxic granulations is rarely seen in contrast to severe ulcerative colitis where both latter conditions are frequent Eosinophilia, as in ulcerative colitis is common, the rate rising to 4 to 8 or 12 per cent in a small number of cases The explanation of the eosinophilia in both conditions is not apparent The attempt to explain the eosinophilia on an allergic basis is not satisfactory, nor are foreign body inclusions a reasonable answer, the eosinophilia is part of the general systemic reaction to the disease The leukocyte counts given by Koster are considerably higher than observed in this series He noted frequent rises to 16,000 or 20,000 or even above this figure This is mainly to be explained by the fact that as a surgeon he saw a greater percentage of cases of acute ileitis It is true that in acute ileitis the total white count is higher and a greater percentage of polymorphonuclear leukocytes is present in the circulating blood a fact that only intensifies the confusion in differentiating acute ileitis from acute appendicitis An increased sedimentation rate of the red blood cells is usually observed, according to Snapper, Pompen and Groen

A moderate often progressive anemia characterizes regional ileitis In advancing cases the hemoglobin reading may range from between 60 per cent and 70 per cent on the Sahli scale lower readings are not unusual even in the absence of gross intestinal hemorrhage In one case in this series the hemoglobin fell to 32 per cent Sahli without evidence of melaena In another case twice operated upon for recurrent ileitis the severe anemia of 16 per cent hemoglobin was explained when the true picture of a primary pernicious anemia became apparent in the blood smears An achylia gastrica was present, reticulocyte response to liver extract was absent in this individual The

pernicious anemia in this case was incidental and probably not related to the regional and recurrent ileitis

Gastric secretory changes in ileitis are unusual One regularly notes a normal type of curve in the fractional test meal, the secretory curve may, however, be low (hypo acidity) Apart from the above cited case complicated by pernicious anemia, only once was achylia gastrica seen in this series

The *general symptoms* of ileitis are those of weakness, loss of strength and loss of weight A material weight loss was noted in 57 cases in this series, in one instance the loss amounting to 50 pounds In the advanced cases, those with intestinal obstruction, and following debilitating operations, the loss of flesh may be much greater and extreme, in terminal cases amounting to emaciation This extreme is, however, unusual The average case may lose 10, 15 or 20 pounds, the patient finds it difficult to regain weight because of the persistent diarrhea and abdominal pain Following successful operative procedure the regain of weight is rapid and ample The loss of strength is not extreme, many patients with mild ileitis are able to continue at their work with little loss of efficiency In one instance, a man in the Armed Forces during the recent war was able to continue an active service for three years after the onset of diarrhea which signalized the initiation of the ileitis, the diagnosis then being unrecognizable or unrecognized In a man 71 years of age who complained of anorexia, weakness, moderate diarrhea and a loss of 25 pounds of weight simulating cachexia, the entire clinical picture was *one of masked carcinomatosis Repeated x ray* examinations of the gastrointestinal tract were reported as negative Eventually exploratory operation revealed a *regional ileitis involving 60 cm (24 inches) of terminal* ileum

Retarded growth and delayed secondary sexual maturation was noted only once in this series of regional ileitis Where the higher reaches of the ileum and the jejunum

are involved the interference with growth and maturity will be observed to be much higher

Menstruation is usually regular and maintained in contrast to ulcerative colitis, where amenorrhea characterizes the more severely toxic nature of that disease

Joint pains were present in 4 of this series, the larger joints such as ankle, knee and elbow being usually involved, as is so commonly seen in segmental colitis The small joints of the hands and feet are spared in ileitis Clubbing of the fingers of the hands occurred four times in this series

The nervous, or rather, psychic manifestations of this disease are sometimes so manifest that they overwhelm the true somatic manifestations This occurred in 10 of this series of cases, probably much more often In 6 of the cases, the onset of symptoms occurred while in active service in the Armed Forces Most of the cases were regarded as psychoneurotic following exposure to battle, or due to bomb shock some were classed as nervous diarrhea, or as food poisoning In 2 of the cases, the diagnosis was properly made by the Army During the war I had ample opportunity to visit neighboring camps in the vicinity of New York City and was shown many correctly diagnosed cases of ileitis In civilian life, 4 cases were treated as depressions or as neurasthenia, 2 of them in institutions for mental care The evident psychic and nervous symptoms that accompany ileitis often lead to delayed recognition of the true cause for the symptoms Of Blackburn s 22 cases, 1 suffered from a true psychosis 4 were referred to psychiatrists for mental treatment when, as he states a routine clinical pathological and radiological investigation would undoubtedly have shown organic disease of the ileum "

However, ileitis can hardly be classed as a psychosomatic disease, occurrences or recurrences do not follow upon psychic shock as evidently as they can be observed in ulcerative colitis with obvious relationship of cause to effect

pernicious anemia in this case was incidental and probably not related to the regional and recurrent ileitis

Gastric secretory changes in ileitis are unusual. One regularly notes a normal type of curve in the fractional test meal, the secretory curve may, however, be low (hypo acidity) Apart from the above cited case complicated by pernicious anemia, only once was achylia gastrica seen in this series

The *general symptoms* of ileitis are those of weakness, loss of strength and loss of weight A material weight loss was noted in 57 cases in this series, in one instance the loss amounting to 50 pounds In the advanced cases, those with intestinal obstruction and following debilitating operations, the loss of flesh may be much greater and extreme, in terminal cases amounting to emaciation This extreme is, however, unusual The average case may lose 10, 15 or 20 pounds the patient finds it difficult to regain weight because of the persistent diarrhea and abdominal pain Following successful operative procedure the regain *of weight is rapid and ample The loss of strength is not* extreme many patients with mild ileitis are able to continue at their work with little loss of efficiency In one instance a man in the Armed Forces during the recent war was able to continue an active service for three years after the onset of diarrhea which signalized the initiation of the ileitis, the diagnosis then being unrecognizable or unrecognized In a man 71 years of age who complained of anorexia, weakness *moderate diarrhea and a loss of 25* pounds of weight simulating cachexia, the entire clinical picture was one of masked carcinomatosis Repeated x ray examinations of the gastrointestinal tract were reported as negative Eventually exploratory operation revealed a regional ileitis involving 60 cm (24 inches) of terminal ileum

Retarded growth and delayed secondary sexual maturation was noted *only once in this series of regional ileitis* Where the higher reaches of the ileum and the jejunum

are involved the interference with growth and maturity will be observed to be much higher

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Physical Examination

The two outstanding features in the physical examination of the cases of regional ileitis are (1) an abdominal mass and (2) evidence of fistula formation external and internal

The abdominal mass (observed in 76 cases in this series) is usually found in the right lower quadrant of the abdomen, in an anatomic area corresponding to the inner surface of the cecum The mass varies in size from that of a finger, to that of a lemon, a large orange, occasionally even larger The mass is usually fixed to the posterior peritoneal wall, to the cecum, or to the anterior abdominal wall, particularly when an external fistula is present leading anteriorly from the mass Tenderness on palpation is constantly present, when the mass is small and in its typical site it is with difficulty differentiated from a spastic cecum The mass consists materially of the inflamed terminal loop of ileum and of adherent loops of nearby ileum or of cecum, ascending colon or sigmoid

On separating the segments of the mass at the operating table, it will usually be seen that the intestinal loops are adherent because of single or multiple intercommunicating fistulous tracts The mass, particularly when adherent to the dome of the urinary bladder, may be apparent in the lower mid abdomen, in one instance simulating a urachus cyst In another instance the loops of ileum were adherent to and drawn over by the sigmoid colon, the mass being palpable to the left of the midline of the abdomen

The most common seat for the mass is low in the right lower quadrant of the abdomen, palpable frequently by rectal or vaginal pelvic examination or by the bimanual technic This fact is easily explainable the position of the terminal ileum is dependent from the cecum Testut places the cecum below the pelvic inlet in 15 per cent of males and in 30 per cent of female bodies In the upright position, the cecum and loops of terminal ileum fall into the pouch of Douglas in the male and between the uterus and the rectum in the female Very often these loops lie directly on the pelvic floor (fig 11) supported by the Levator Ani

muscle Monks found the terminal ileum to be in the pelvis in more than 50 per cent of his studies In our own

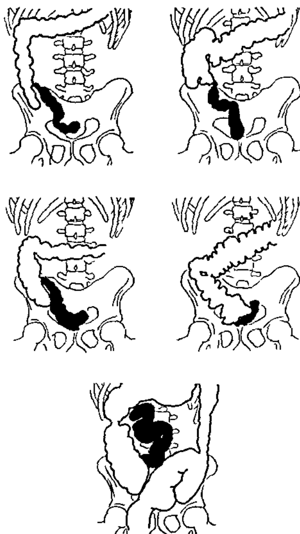


Fig 11 —Anatomic Position of the Normal Terminal Ileum (1) Usual position of cecum and ileum (2) high cecum ileum to pelvis (3) low cecum high medial implantation of ileum (4) complete descent cecum and ileum in pelvis (5) exceptional position of terminal ileum abrupt ascension The majority of cases fall within groups 1 and 3 Reprinted from Radiology 3 32-330 1939

radiographic studies, made to determine the position of the normal ileum, it was found (Crohn and Yarnis) that in 150 control normal cases descent of the cecum and terminal ileum into the lower pelvis occurred in 28 per

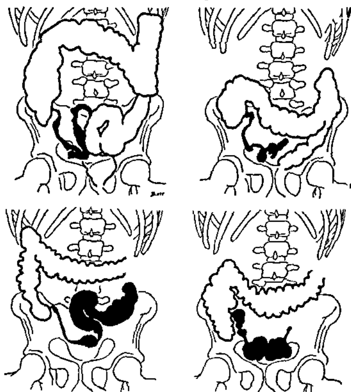


Fig 12—Anatomic Position of the Diseased Terminal Ileum as Classified from a Study of 25 Cases of Terminal Ileitis The weight of the diseased loop carries it so as to lie on the pelvic floor Reprinted from Radiology *33* 325–330 1939

cent of the observed cases in that series In the pathologic ileum (25 cases of terminal ileitis) the terminal affected loop of ileum was found in the pelvis in all cases, in fact on the floor of the pelvic cavity (fig 12) It is apparent that the soggy weighted diseased ileum descends low down in the right lower abdominal quadrant and being even heavier than normal in weight occupies almost uniformly the pelvic inlet The mass of ileitis is then found and easily palpated

by bimanual technic in the fossa of Douglas Only when adherence to other organs takes place is the mass felt other than in the right lower abdominal cavity When fistulous tracts burrow into and through the apposed base of the mesentery, the necrotic process may cause a diffuse suppurative mesenteritis which participates in and increases the size of the inflammatory mass

Apart from the abdominal mass and the demonstration of characteristic fistulas the physical examination of the cases of ileitis is likely to be negative Enlargement of the spleen was noted four times, clubbing of the fingers four times not necessarily in the same patient Both manifestations indicate the degree of general body affection as part of the localized intestinal process

Erythema nodosum on the anterior aspect of the lower extremities was noted once in acute ileitis and twice in chronic regional ileitis This phenomenon, which is so much more prevalent in ulcerative colitis possibly links the two diseases in a common etiological factor

OBSTRUCTIVE PHENOMENA

Intestinal obstruction occurred in 10 instances in this series of 222 cases usually late in the course of the disease Twice in this series it was an early, in fact the presenting symptom at the onset in the other cases it indicated a long standing chronic inflammatory process eventuating in chronic cicatricial stenosis of the bowel at the site of the lesion Dickinson and Zimmerman report a single case with intestinal obstruction as the initial presenting symptom Sherill and Hall indicate 2 cases with obstruction as the initial phenomenon though both were old chronic cases Jackman reported 2 cases of hypertrophic enteritis as a cause of intestinal obstruction both cases of the acute type in both of which the terminal ileum was perforated during the operative manipulations

Occasionally the obstruction may be due to angulation and kinking of a loop of bowel by peritoneal adherence or by ileo ileal fistulation Loops of distended intestines

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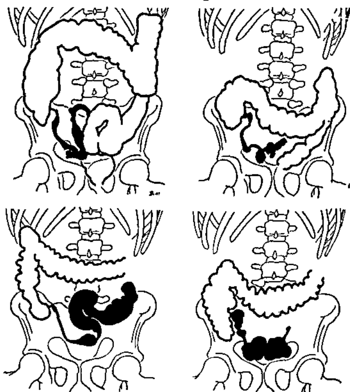


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5 Fistula Formation in Regional Ileitis

FISTULA FORMATION is the most constant clinical and pathologic phenomenon in ileitis These intestinal fistulas are of three types

1 Fistulas to the anterior abdominal wall

2 Internal fistulas between loops of bowel and adherent hollow viscera

3 Rectal and perirectal fistulas

Fistulas to the anterior abdominal wall are among the most common types of fistulation and occur exclusively in the site of the scar of a previous laparotomy The antecedent operation in most of the cases (30 6 per cent) was an appendectomy We encountered 36 instances of anterior wall fistulas all of them in the appendectomy scar or in the scar of a previous exploratory laparotomy Fistulas to the abdominal wall are infrequent after simple appendectomy for acute appendicitis (Ginzburg) According to Colp in 2840 cases of acute appendicitis abdominal wall fistulas were found only 33 times an incidence of 1 1 per cent only 3 required reoperation Clark and Dixon in 44 cases of regional enteritis found 9 external fecal fistulas one of which passed feces and gas through the urethra Four of these 9 patients also had intraintestinal fistulas one a fistula to the urinary bladder

In some of the instances of ileitis not a single but multiple fistulas were present in one case 4 anterior wall fistulas in several scars of eight previous laparotomies (Crohn) [58] These fistulas occur usually within a few weeks of the apparent healing of the operative scar The scar

may be seen through the thin abdominal wall, visible peristalsis is not uncommon and is accompanied by severe abdominal cramps and borborygmi A scout film of the abdomen will show puddling and fluid levels Vomiting may be present in the more severe stenotic phases The obstruction can usually be temporarily alleviated by the use of the Miller Abbott tube

Postoperative intestinal obstruction, such as characterizes many cases of intestinal resection or short circuiting operations is unfortunately only too frequent but fortunately does not occur as frequently as in reconstructive surgery for ulcerative colitis

rise to some speculation as to their nature They are apparently lytic rather than infectious in type They traverse large areas of mesentery and distal fascial planes without giving rise to infection terminating their course by finding an exit point somewhere on the surface of the body They are lytic or proteolytic the activated intestinal or pancreatic enzymes of the fecal chyme slowly digesting their way through planes of fascia and muscle to exit on

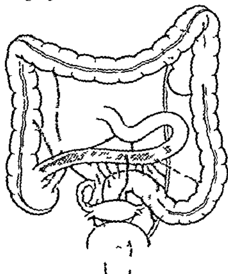


Fig 13—Fistulation Terminal Ileum to any Adjoining Hollow Viscera Note termination in such unusual sites as right fallopian tube left ureter body of uterus

the body wall Such fistulas become infected and suppurate only as a result of skin bacterial contamination at the point of exit from the abdominal cavity

INTERNAL FISTULAS (FIG 13)

The mechanism of formation of internal intestinal fistulas is identical with that of external abdominal wall fistulas These tracts originate in the sodden leaking ulcerated terminal ileum usually on the side of mesenteric attachment They traverse the mesentery of the small bowel and terminate in an adjacent loop of small intestine,

becomes reddened, and inflamed at a localized area, a low grade fever becomes apparent with regional pain and tenderness An abscess forms and either breaks spontaneously or is incised, following which fecal drainage occurs and a chronic fecal fistula is established In some instances the abdominal wall fistula occurs only months or years later, two years, four years and in one instance eight years after a presumably successful resection for terminal ileitis The eight intervening years were marked by excellent health until the appearance of the fistula signalized a recurrence of the ileitis

These external wall fistulas are apparently very facile of creation, in two instances just knicking the diseased bowel wall accidentally during operation resulted in immediate fistula formation in the healing incision, even though great surgical care was immediately exercised in suturing the cut in the wall of the ileum

Spontaneous fistulas to the abdominal wall without a *previous laparotomy have not been observed* *But unusual* exit sites for external fistulas are occasionally noted Multiple external fistulas to the inguinal region have been noted twice, at least four fistulas in one instance, there being no previous operative scar Hurst has noted a fistulous tract originating in the ileum and pointing downward and infiltrating the extraperitoneal tissues in the right groin Brown and Donald reported 47 cases with fistula formation out of a total of 178 cases an incidence of 26 5 per cent This is a higher incidence of fistulation than encountered in this present or in most of the current literature They further state that fistula formation occurs invariably only after surgical procedures

Fistulas to the lumbar region have been seen three times twice by the author and once mentioned and reported by Snapper, where a series of external fistulas occupying the right lumbar area were observed expelling vegetable matter and fecal content The fistulas were traced to a terminal ileitis The linear extent of these intestinal fistulas gives

rise to some speculation as to their nature They are apparently lytic rather than infections in type They traverse large areas of mesentery and distal fascial plane without giving rise to infection terminating their course by finding an exit point somewhere on the surface of the body They are lytic or proteolytic the activated intestinal or pancreatic enzymes of the fecal chyme slowly digesting their way through planes of fascia and muscle to exit on

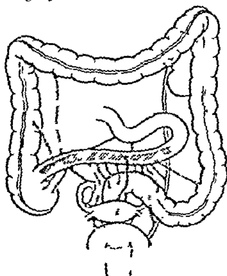


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INTERNAL FISTULAS (FIG 13)

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in any segment of the large bowel, or in any adjoining hollow intra abdominal viscus, such as ureter, urinary bladder, uterus or fallopian tube

The internal fistulas were noted in 23 of our series (approximately 10 per cent) though the incidence of such internal fistulas would appear in practice to be much higher



Fig 14—Diagrammatic Sketch Fistulation Terminal Ileum to Small Intestine and Cecum

Variations of these internal fistulas may be listed as in table 6

TABLE 6—*Variations of Internal Fistulas*

Terminal ileum to	
sigmoid	6 instances
cecum	3 instances
ascending colon	3 instances
other loops of ileum	instances
duodenum	instances
urinary bladder	4 instances

Other variations are ileum to right ureter, to left ureter to urinary bladder, to the intra uterine cavity to the right fallopian tube

On two occasions the opening of the fistula into the sigmoid colon was seen by sigmoidoscopy. In another instance the fistula which broke into the right fallopian tube gave rise to a salpingitis discovered inadvertently by a gynecologist operating for supposed adnexal inflammation. The discharge of the proteolytic content of the fis-



Fig. 13.—Combined Ileitis (Terminal) with Involvement of the Ascending Colon and Cecum. Note fistulous tracts between ileum and base of cecum. Meckel's diverticulum not involved. (Involved segment to the left; Meckel's diverticulum inverted.)

tulous tract into any hollow viscus usually terminates its course.

Probably the most common of all these internal fistulas are the ileocecal variety; they are readily demonstrated at the operating table (figs. 14, 15, 16). Many or most of these fistulous tracts are notable and visible in the preoperative radiographic films provided they are diligently sought after (figs. 17 and 18). The fine lines seen with a magnifying lens emanating from the diseased ileum indicate potential fistulas

(fig 18) These are frequently seen overlying the dome of the urinary bladder and creating urinary symptoms, actual gross fistula exit into the urinary bladder is rare in ileitis,

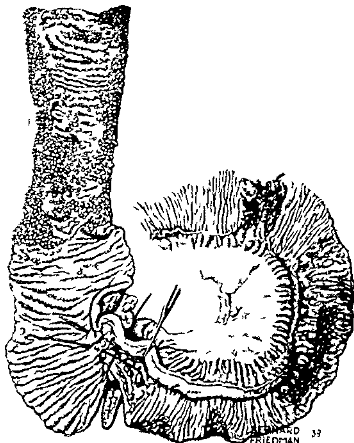


Fig 16—Terminal Ileitis Multiple Fistulas Regional Skip Areas throughout Ileum and Jejunum A S 21 years male Regional colitis Picture after three months of medical treatment

much less common than are such similar fecal fistulas which arise in a sigmoid diverticulitis Forbes and Duncan report an interesting case of ileitis in which a large fistula existed between the terminal ileum and the urinary bladder, the patient passed gas and fecal material per urethra Ileo

transverse colostomy without transection of the ileum was performed but the intestinal symptoms and those of the ileo vesical fistula persisted. At a second operation, the ileum distal to the anastomosis was transected as the sole procedure except for a temporary ileostomy of the distal ileal loop Within four months the patient gained 25



Fig 17—Terminal Ileitis Fistula, Ileum to Sigmoid

pounds in weight was free of symptoms and the dysuria and passage of gas and feces per urethra had disappeared Unfortunately a severe recurrence of the ileitis occurred after the date of publication of their article In another case cited by these authors an ileo vesical fistula persisted for some time in spite of an ileo colostomy This fistulous tract was resected broke down again with the secondary formation of an additional fecal fistula but eventually both fistulous tracts healed with subsidence of all symptom

Brown and Donald culled from a review of 178 cases of regional enteritis with complications of fistulas the variations in the site of the disease as shown in table 7

Table 7—Site of Regional Enteritis with Fistula (Brown and Donald)

	Fistulas	
Site of disease	*Internal*	*External*
Jejunum—5 cases	0	0
Upper ileum—8 cases	0	1
Lower ileum—99 cases	4	18
Ileum and Colon—66 cases	4	14



Fig 18—Regional (Terminal) Ileitis with Vesical Symptoms Multiple Minute Formation of Fistula

The exemption of the jejunum to fistula formation is thus seen, the lower ileum is the site of most of the internal and

external fistula formation Pugh describes fistulation in six of his cases the fistulas being identified as in table 8

TABLE 8—Fistula from Ileum (Pugh)

Ileum to	
sigmoid	[illegible]
cecum and jejunum to cecum	1
sigmoid to urinary bladder	1
cecum	1
transverse colon	1

PERIRECTAL FISTULAS

In 1934, Bissell published a case report of terminal ileitis in which multiple rectal fistulas occurred as a complication of the intestinal disease He felt that the presence of the inflammation of the ileum in the cul de sac could easily have given rise to a rectal abscess and persistent rectal fistula In 1938 the diagnostic significance of perianal, rectal and recto vaginal fistulas was emphasized [190] In that publication 20 cases of perirectal fistulation were noted in a group of 110 cases of ileitis an incidence of 18 2 per cent This was almost equal to the number of external abdominal wall fistulas (12 cases) and internal intestinal fistulas (11 cases) combined as shown in that series

In the present series of 222 cases of regional ileitis, perirectal abscesses and fistulas were noted 39 times an incidence of 17 5 per cent this does not include 3 instances of recto vaginal fistulation The total number is somewhat below the combined number of external and internal intestinal fistulas in this present series (59 cases 26 5 per cent)

Jackman and Smith in 1943 recorded at the Mayo Clinic 36 cases of anal abscess or fistula in a group of 114 cases (31 6 per cent) a figure high above those in this series They included those cases having had a history of operation for anal fistula within a three year period prior to their initial visit Eight of the series of 114 cases came to the Clinic primarily because of anal fistula the intestinal disturbance being so mild as to have been overlooked

METHOD OF ANAL FISTULATION

Either of two methods may explain anal suppuration (1) Most of these fistulas occur as a result of infection in

the rectal crypts of Morgagni above the anal sphincter, the contaminated fecal infectious material being transported thereto by the propulsion of the fecal column The infection of the crypts gives rise to a perirectal abscess or an ischio rectal abscess which opening simultaneously on the surface of the buttock and within the anal canal forms a permanent fistula When the abscess localizes anteriorly in the female, it may break simultaneously through the

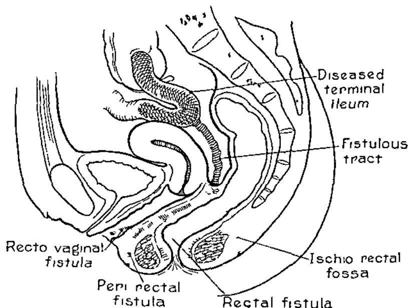


Fig 19 —Gravity Fistula Route of Direct Fistulation from Terminal Ileum to Perirectal Spaces This type i comparatively rare in compari on with the type which originates in transported infection with lodgement in the crypts of Morgagni

perineal body into the vagina and posteriorly into the rectum, forming a recto vaginal fistula

This type of local rectal infection in ileitis is almost identical with that seen in ulcerative colitis In both, the internal opening of the fistulous tract is just within the anal margin, in the recto vaginal fistulas the anterior opening is just within and above the fourchette, constituting a small opening which emits a thin fecal leakage

(2) The second method of fistulation to and about the anus and perineum is more problematic This fistulous tract is considerably more circuitous proteolytic material escapes from the porous terminal loop of ileum lying heavily on the pelvic floor The material seeps downward through the pelvic peritoneal reflection and the retroperitoneal fat and burrows through the pelvic fascia following the planes of the levator ani muscle (fig 19) The material makes its exit into the rectum above the sphincters, or, piercing the slinglike attachments of the fibers of the levator ani makes its exit at the perianal margins The ischio rectal fossa may be contaminated forming an abscess which will reveal itself as a perirectal fistula communicating internally with the rectum Attempts to follow such long fistulous tracts are difficult lipiodol injected into the tract from below will ascend for several inches but will be lost somewhere in the pelvis a streak of barium following a radiographic study may be seen pointing downward in the same direction A direct and continuous path has not been unequivocally demonstrated except in one case in the literature where at autopsy the continuity of the path was clearly dissected (Patricelli)

The diagnostic significance of perianal fistulas has not been sufficiently appreciated they may occur one to fourteen years before the onset of active diarrhea and abdominal pain constituting the early prodromal manifestations of the disease

It is a fair statement to make as a generalization that suppurative perianal fistulas in the presence of diarrhea indicate a pathologic inflammatory process somewhere in the intestinal tract These fistulas occur with great frequency in ileitis, ulcerative colitis and in intestinal tuberculosis They do not occur in nervous gastrogenous, pancreatic allergic or thyrogenic diarrheas Exceptions to this general rule have not been noted however for the sake of scientific accuracy it would be better to keep an open mind though the general truth of the statement will probably continue to operate

6 The Course in Regional Ileitis

REGIONAL ILEITIS may begin as an acute phase of the disease, or it may be first observed as an acute exacerbation of a clinical process which has been overlooked, in the vast majority of cases it comes under observation as a disease of great chronicity The acute case, simulating acute appendicitis (except for the presence of diarrhea as a symptom) resolves in 25 per cent of the cases without further evidence of recrudescence The remainder of the acute cases subsides spontaneously, usually in spite of the laparotomy and customary appendectomy and lapse into the low grade typical chronic course of the disease

The course of long standing chronic regional ileitis is one of great chronicity Spontaneous remissions that endure for years may occur, during which remissions the diarrhea will abate or be absent, the temperature remain normal, appetite be preserved and nutrition be only slightly impaired Except for a slight and slowly progressive loss of weight, mild persistent anemia and occasional short bouts of diarrhea and abdominal pain, the patient may follow a normal career of physical well being and school or occupational activity As the disease progresses in the intestinal tract the periods of activity will be greater and last longer the remissions become shorter In time either the continuous diarrhea or the loss of weight and strength will indicate the progression into a more severe phase of the disease Eventually the onset of obstruction (10 cases) will supervene with abdominal pains vomiting, and the ability to feel an abdominal mass on palpating the abdomen

At any time in the course of the disease a peri rectal abscess or a fistula in the scar of the abdominal wall may supervene

In the continued study of chronic regional ileitis with the assistance of radiographic observation, it will be noted that three variations in the course must be considered In the first group, spontaneous healing of the lesion with disappearance of all radiographic evidence will supervene This occurred in 13 of this series of 222 cases of regional ileitis The second group is constituted of cases in which anatomically the lesion remains static, usually localized to the terminal ileum progression upward of the pathologic process cannot be radiographically demonstrated In the third group the lesion is obviously a progressive one and continues to spread mildly either continuously or by skip lesions until the upper reaches of the ileum or the jejunum become involved

Group 1

Chronic long standing regional ileitis with spontaneous healing (13 cases) It was surprising to note the fact that spontaneous healing could take place in regional ileitis this even in cases where internal fistulation had been radiographically demonstrated In 5 of these cases the diagnosis had been first observed and confirmed at the time of previous appendectomy Some of the details of these 13 cases are of great interest particularly since spontaneous resolution of the inflammatory process is so unusual

Case 1 E S Male Age 27 years Six years of pain and diarrhea At exploratory operation in 1940 3 feet of terminal ileum were observed to be involved the operation was restricted to the exploration Four years later the patient was well with one or two formed stools and a regain of weight (x rays were completely negative)

Case 2 J B (Serial No 19) Male 4[illegible] years of age For two years previously the patient had suffered with loose and frequent bowel movements fever up to 10 F predefecation cramps and a loss of 25 pounds of weight At the radiologic examination a typical terminal ileitis involving the last 18 inches of ileum was easily discernible (1943) The course of the disease for four years was benign practically nonsymptomatic An acute incident resembling a subacute

intestinal obstruction supervened (1947) but subsided without operation under medical treatment The patient has remained well to date

Case 3 A H (Serial No 70) Male, aged 42 years Fifteen years previously the patient underwent an appendectomy The wound suppurated for four months Two years later the wound broke open establishing a fecal fistula which later closed spontaneously He remained well for thirteen years except for slight attacks of abdominal pain and mild diarrhea When seen in 1942 he was in good health the radiologic examination disclosed a string sign involving the terminal 12 inches of the ileum On physical examination a suggestion of a mass was palpable under the lower right rectus muscle The follow up two years later reported the man as in perfect health and free of all symptoms

Case 4 J C Female age 27 years Appendectomy 1938 For six years following this operation continued pain regular bowel movements Marriage and birth of two healthy children without complications or difficulties Subsequent onset of diarrhea Subsidence of all symptoms but persistence of radiographic evidence of disease involving the distal 2 feet of the terminal ileum Regarded as well in view of subsidence of all clinical symptoms for the last two years (1946)

Note August 1948—exacerbation of pain and diarrhea, suspicion of low grade obstruction The reversal of the prognosis in the case from that of apparent cure to active symptoms suggesting surgical intervention is most disappointing

Case 5 H A Female Terminal ileitis fistula ileum to cecum No operation Three years later mass had disappeared, internal fistula no longer visible patient well Radiographic examination negative

Case 6 S F (Serial No 50) Female age 47 years widow At 18 years of age appendectomy intestine seen to be inflamed Twelve years ago cholecystectomy for multiple biliary calculi Two years abdominal cramps diarrhea four to five watery movements daily Physical examination negative when first seen in 1944 Radiographic examination marked inflammatory involvement of terminal two loops of ileum Follow up three years later well asymptomatic Persistent evidence of fibrotic lesion in terminal ileum was demonstrated by recent radiographic examination

Case 7 I C (Serial No 29) Male age 16 years Had been operated upon when 8 weeks of age for congenital pyloric stenosis Three years ago had been operated for supposed intestinal obstruction due to adhesions(?) For the last two years following upon this operation (1944) had suffered bouts of diarrhea and abdominal pain with occasional febrile exacerbations The radiographic examination at that time was reported as negative Radiographic study in 1946 distinct irregularity of terminal ileum Subsequent and objective improvement under sulfathaladine therapy When last seen October 1947 well and symptom free

Case 8 E K (Serial No 209) Female age 39 years married three healthy children For five years has suffered with recurrent diarrhea

and periumbilical pains loss of 9 pounds of weight One year ago small bowel barium series showed a mild irregularity of the terminal ileum Repeat series (1945) by both barium enema and barium meal one year later showed definite and distinct lesion involving several loops of the terminal ileum A third radiographic study a year later (1946) demonstrated a definite involvement of the terminal twenty inches of the small intestine Marked clinical improvement regain of weight cessation of diarrhea Radiography almost two years later December 1947 revealed practically a normal terminal ileum

Case 9 M I (Serial No 213) Male 21 years of age Served in U S Navy during the war from 1943 to 1946 Onset of symptoms following the explosion of a bomb on the deck of a destroyer thrown some distance across the deck Developed abdominal pains nervousness fear of going below decks anorexia Sharp cramplike abdominal pains diarrhea three to four loose daily movements Hospitalized in Naval Hospital as case of psychoneurosis no intestinal radiographic studies made Radiographic studies 1946 strongly indicative of terminal ileitis Repeat radiographic studies by barium meal and barium enema showed involvement of terminal 12 inches of ileum Follow up 1947 and February 1948 patient well and free of symptoms

Case 10 S C Male 23 years of age single Appendectomy abdominal wall fistula spontaneous closure of fistula Radiographic evidence of terminal ileitis 1944 Well (1947)

Case 11 A G Female 23 years of age Appendectomy abdominal wall fistula Spontaneous closure of fistula Barium meal demonstrates inflammatory lesion of terminal ileum 1944 Follow up 1947 well and free of symptoms

Case 12 H F (Serial No 38) Male age 62 years Seen in 1939 for first time Ten year history of occasional attacks of watery diarrhea associated with mild abdominal pain Physical examination revealed vague mass under lower right rectus muscle No fever Loss of 15 pounds of weight Radiographic examination revealed typical string sign involving terminal 16 inches of ileum The patient continued spontaneously to improve is now free of symptoms and continued so to this date nine years later (December 1947)

Case 13 E G (Serial No 63) Female age 19 years single Ten month history 5–6 feet of ileum involved in x ray Active diarrhea and fever Three years later only 1–1½ feet of ileum involved by radiographic study Three years later patient well radiographic examination negative

It will thus be observed that in a minority of fortunate individuals an apparent spontaneous cure is possible fistulas internal and external are under exceptionally favor

Since this list was compiled this patient has been operated for recurrence of his supposedly healed lesion

intestinal obstruction supervened (1947) but subsided without operation under medical treatment The patient has remained well to date

Case 3 A H (Serial No 70) Male aged 42 years Fifteen years previously the patient underwent an appendectomy The wound suppurated for four months Two years later the wound broke open, establishing a fecal fistula which later closed spontaneously He remained well for thirteen years except for slight attacks of abdominal pain and mild diarrhea When seen in 1942 he was in good health, the radiologic examination disclosed a string sign involving the terminal 12 inches of the ileum On physical examination a suggestion of a mass was palpable under the lower right rectus muscle The follow up two years later reported the man as in perfect health and free of all symptoms

Case 4 J C Female age 27 years Appendectomy 1938 For six years following this operation continued pain regular bowel movements Marriage and birth of two healthy children without complications or difficulties Subsequent onset of diarrhea Subsidence of all symptoms but persistence of radiographic evidence of disease involving the distal 2 feet of the terminal ileum Regarded as well in view of subsidence of all clinical symptoms for the last two years (1946)

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apparent health and in spite of apparent surgical cures. The final word on the life history of the disease as pertains to self healing may require future elaboration.



Fig 21 —Seven Months after Onset

Group 2 Chronic Regional Ileitis without Progression

The exact percentage of cases in this group cannot be stated since comparative radiographic studies over the course of years is not often capable of fulfillment (figs 20–22). A sufficient number of cases have, however, been observed to allow the inference to be drawn that in many cases observed over the course of years radiographically the lesion remains stationary. This applies even in cases where skip lesions are already demonstrable. As for example

Case 1 I S (Serial No 216) Female age 32 married First seen in November 1947 Nine years ago incision and drainage of a recto vaginal fistula Four years ago appendectomy For nine years patient had been suffering with diarrhea and abdominal cramps four to five watery stools daily Radiographic studies made three years ago showed

able conditions, capable of self healing. Restoration to normal health and well being seems possible. Wilensky has published such a case of spontaneous healing in non specific granuloma of the terminal ileum, although his conclusions are based purely on radiographic readings; diar-



Fig. 20, 21 and 22—Terminal Ileitis. Conservative Medical Therapy for a Period of a Year and Two Months. Note absence of progression of lesion. Restriction of process to terminal 12 inches of ileum.
Fig. 20.—At Onset.

rhea had never been present in his case and there were no corroborative surgical exploratory findings to confirm the statements in this one case. These observations on self healing are made with the reservation that relapses have been noted even after as much as nine to sixteen years of

because of mild but persistent symptoms a barium meal was undertaken This radiographic examination revealed involvement of the terminal 8 inches of ileum (1944) Two years ago (1946) obstructive phenomena now became apparent for the first time One year later the patient underwent an exploratory laparotomy because of persistent abdominal pain and diarrhea An ileo transverse colostomy with transection of the ileum was performed for a cicatrizing and contracting ileitis involving the terminal 8 inches of the ileum In other words



Figs 23 24 25 and 26—Series of Radiographs Illustrating Progress of Lesion in a Case of Regional Ileitis Observations extend for little more than one year

Fig 23—Only the Terminal Ileum Involved

during *four years of observation the lesion remained limited to that* anatomic area which was present when first properly observed namely the terminal 8 inches of ileum

Case 3 F F (Serial No 202) Female single age 34 years First seen in 1946 Fifteen years ago had been operated for a rectal fistula Exploratory operation revealed the terminal 8 inches to be involved in what was then *regarded as intestinal Hodgkin s disease* A localized resection was undertaken Mild intestinal diarrhea continued for th

involvement of 5 cm (2 inches) of the terminal ileum Similar radio graphic studies carried out two years ago showed identical involvement of the last two inches of terminal ileum Three months ago a barium meal demonstrated involvement of the last 2–3 inches of terminal ileum with the finding of a significant 'string sign A tender pipe stem like mass was now palpable in the right lower quadrant of the abdomen



Fig 22—After One Year and Two Months of Medical Treatment

This case is typical of the stationary or nonprogressive form of terminal ileitis

Case ~ D 4 (Serial No 10) Male age 15 years First seen in April 1943 For the previous ten months had suffered with recurrent attacks of diarrhea and abdominal cramps the pains occurring just before defecation and relieved by that act He had lost 20 pounds of weight in that period A mild secondary anemia existed (hemoglobin 72 percent) The original x ray examinations failed to visualize the terminal ileum and the correct diagnosis was missed One year later

These cases without extension of the disease over the course of years seem to lend themselves best to surgical intervention. While late intestinal obstruction is often characteristic of this chronic type, recurrences after operation are less likely to occur. This group should be the most satisfactory for surgical cure. In one case the lesion was recognized at exploratory operation eighteen years ago;



Fig. —Two Months Later. More Extensive Involvement of Whole Lower Ileum

the true nature was not recognized and no further surgical intervention was attempted. The disease lay dormant and presumably asymptomatic. Recurrence of diarrhea and a positive x-ray picture led to operation and resection of the persistent and unextended lesion in the terminal ileum.

Group 3. Chronic Regional Ileitis with Progressive Extension

These are the cases in which the study of the life history of the disease over a course of years reveals active progression of the lesion in an oral direction. Again there

last fifteen years At exploratory operation performed in 1946 the identical section of ileum namely 8 to 10 inches was involved a short circuiting operation ileo-sigmoidostomy with transection of the ileum above the diseased area was carried out

Case 4 I B (Serial No 197) Male age 39 years First seen in 1946 For ten years had had intermittent attacks of diarrhea and abdominal cramps Eight years ago had been operated upon for a rectal fistula For the last two years had severe recurrent attacks of abdominal cramps with fever up to 101 2 F the cramps at times being so severe as to require hypodermatic administration of morphine Two



Fig 24 —Six Month Later Extension of Progress to Involve Approximately Two Terminal Loops of Ileum

years ago radiographic examinations supposedly demonstrated only a spastic colon A progressive loss of weight amounting to 39 pounds had been observed during the last ten years A radiographic examination performed one and a half years ago showed suggested involvement of the terminal loop three to four feet of the small bowel Six month ag the patient underwent an exploratory laparotomy because of persistent symptoms of fever and diarrhea At the operation the identical involvement of the last 3 to 4 feet of ileum was observed with the additional finding of a fistulous tract between terminal ileum and sigmoid In spite of the mucosal type of ileitis here demonstrated and the lack of cicatrization or the identification of a typical string sign, the disease when finally explored by operation had not extended beyond the original site of involvement A short circuiting operation was performed with apparent excellent results

It is likely that this is the so called mucosal or submucosal type of case that gives the disappointing results after surgical therapy, the rapid progression probably indicates that much more of the upper bowel is involved than is demonstrable on the x ray plates

In the chronic case of regional ileitis remission of long periods may be observed such periods covering months and many years have been noted up to five to ten years between recurrences of diarrhea and fever In one case the onset of symptoms dated eight years after a previous appendectomy for supposed "chronic appendicitis" In the later stages of the disease, the symptoms become increasingly severe, the recurrences more frequent, and of longer duration, until continuity of severe complaints causes complete disability

are insufficient personal observations to allow of any percentages to be offered, but an occasional observed case is illuminating As examples

Case 1 M H Male age 42 In 1935 exploratory operation for terminal ileitis fistula in ano Eight to 10 inches then involved no resection In 1943, eight years later whole ileum involved up to jejunum Hypoproteinemia marked emaciation

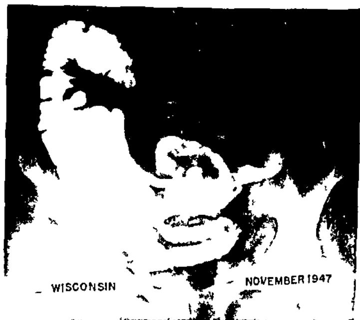


Fig 26—Five Months Later Involvement of the Whole Ileum This is the mucosal or submucosal type of ileitis with progressive extension

Case 2 (Figs 23–26) M W (Serial No 222) Female married 31 years of age First seen June 1947 For the last 13 months suffered with mild diarrhea and attacks of bloating and of abdominal cramps *She has been constantly uncomfortable after eating* She has sustained a loss of 30 pounds in the last six months The dates and the results of the various radiographic examinations were as follows October 1946—8 to 10 inches of terminal ileum involved March 1947—10–12 inches of terminal ileum involved June 1947—18 inches of terminal ileum involved December 1947—30 inches of terminal ileum involved

In this last case, in which the successive radiographs were present for comparison, the oral progress of the lesion was capable of clear demonstration (figs 23–26)

the form of melaena, twice hematemesis was noted Follis quotes a case with repeated profuse and massive hemorrhage passed by the bowel (melaena) Two previous x ray examinations had been negative Eight transfusions were required to control shock Eventually, at operation, 27 inches of ileum were resected with cure Galambos and Mittelmann cite a case of atypical terminal ileitis in which gastric hemorrhage and melaena dominated the clinical picture and led to the presumptive diagnosis of a peptic ulcer Yunich and Crohn reported the case of a 55 year old male in which the onset of symptoms was ushered in by two massive intestinal hemorrhages in the form of melaena producing syncope and collapse The second hemorrhage was almost fatal

It is difficult to explain hematemesis when it occurs In the 2 cases in which such a phenomenon was seen in this series, the diagnosis of regional ileitis was confirmed by exploratory operation These both were cases in which the terminal ileum was involved, no higher segment of ileum or jejunum being implicated

General Complications

In this series of cases of ileitis, duodenal ulcer was noted five times cholelithiasis three times and acute cholecystitis was encountered once during an operation for terminal ileitis Regional enteritis involving a Meckel s diverticulum has been observed (Horn and Rhoads) in one case with perforation at the base of the sac In my own series I have once seen Meckel s diverticulum involved in a skip lesion In another case a Meckel's diverticulum causing low intestinal obstruction by torsion was clinically preoperatively confused as a case of ileitis Patricelli also mentions a case of regional ileitis with Meckel s diverticulitis with fatal outcome

Some general complications which occur are actually incidental and not related to the disease Thus this series includes 4 cases with chronic rheumatic heart disease one

7 Complications of Regional Ileitis

Perforation of Intestine

ACUTE FRANK PERFORATION with generalized peritonitis is extremely rare, but can occur. Slow walled off perforation is manifest, particularly in the acute instances. In the chronic cases, on laparotomy, it is not uncommon to find a walled off abscess about the inner surface of the terminal ileum, limited by the neighboring loops of ileum and the mesial wall of the cecum, the whole being agglomerated in one confused mass. Upon separating the loops of involved ileum there may be a gush of a small quantity of pus. The neighboring loops are covered with fibrinous shraggy peritoneal deposit, a small quantity of inflammatory cloudy fluid may be present in the peritoneal cavity (300–400 cc). The granulomatous low grade type of infection with concomitant fibroblastic reaction precludes the occurrence of free open perforation with only rare exceptions. Attempts to resect terminal ileitis in the presence of a walled off abscess with localized peritonitis is fraught with a high operative mortality. Arnheim reports acute perforation of five days' standing in a chronic ileitis, death occurred before operative interference. Two perforations of the terminal ileum were observed with localized abscess and peritonitis.

Hemorrhages

Gross hemorrhage was noted in 11 instances in this series usually in the course of the disease occasionally (twice) as an initial symptom. The hemorrhage occurs usually in

the form of melaena twice hematemesis was noted Pollis quotes a case with repeated profuse and massive hemorrhage passed by the bowel (melaena) Two previous x ray examinations had been negative Eight transfusions were required to control shock Eventually, at operation, 27 inches of ileum were resected with cure Galambos and Mittelmann cite a case of atypical terminal ileitis in which gastric hemorrhage and melaena dominated the clinical picture and led to the presumptive diagnosis of a peptic ulcer Yunich and Crohn reported the case of a 35 year old male in which the onset of symptoms was ushered in by two massive intestinal hemorrhages in the form of melaena producing syncope and collapse The second hemorrhage was almost fatal

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with a decompensated right heart on the basis of generalized arteriosclerosis Occasional mention is made of joint pains and arthritis in a case showing spondylitis involving the cervical spine In an unusual case, active pulmonary tuberculosis was present, though the resected ileitis was characteristically of the nonspecific granulomatous type, in this case, too, diffuse involvement of the large joints was noted Infantilism and delayed sexual maturity has already been mentioned One case observed had had a large retroperitoneal or intra abdominal abscess with consequent obstruction of the inferior vena cava

Tetany in regional ileitis is uncommon, occurring more frequently in those cases of diffuse disease involving the upper ileum and the jejunum One case following two resections of the small bowel for recurrent ileitis developed typical carpo pedal spasm Blood calcium in this case was 6 7 milligrams per cent Immediate relief was noted upon injection of calcium gluconate and control of the diarrhea In another case, typical tetanic convulsions were noted with a blood calcium of 3 4 milligrams per cent

Amyloidosis does not occur in any of the cases in this series in spite of the long duration and chronicity of the disease This is due probably to the nonpyogenic nature of the discharge from surface fistulas or in the intestinal flux However, I am privileged to mention one case of generalized amyloidosis which occurred as a sequel to or associated with regional ileitis observed and studied at autopsy (Mount Sinai Hospital New York City, courtesy of Dr Hilliard Cohen) *

Primary amyloidosis of the alimentary tract has been reported by Golden in a Negress observed for 16 years whose presenting symptom was hematemesis dyspnoea and ortho

In the recent article by Olsan and Sussman 3 cases of amyloidosis associated with or secondary to regional ileitis are recorded The amyloid involves various viscera throughout the body and is a prominent factor only in the one case which is identical with that about to be published by Cohen and Fishman (personal communication)

pnea At autopsy, the stomach, duodenum and terminal ileum were all involved, the liver spleen kidneys and adrenal were free of amyloid This however, is different from true primary regional ileitis, in which the systemic amyloidosis is a sequel or a complication In primary systemic amyloidosis, the gastrointestinal tract may be involved as may any other organ involvement of the arterioles and of the stroma occurs frequently in the intestine However systemic amyloidosis secondary to ileitis or nonspecific ulcerative colitis is extremely rare (Koletsky and Stricker, Moschcowitz)

Gaucher's disease was seen in a case of ileitis as an incidental finding Pernicious anemia was seen in one case in this series (serial No 73) in a man 54 years of age who had undergone a short circuiting operation for regional ileitis followed promptly by a recurrence of diarrheal symptoms At a second operation the original site of the disease, the terminal ileum and the ascending colon were resected but no recurrence of the disease process in the new proximal ileum was noted An unusually severe anemia and emaciation followed this operation Two years later the blood count revealed a true primary pernicious anemia Hemoglobin 26 per cent RBC 1,400,000, WBC 2,650 cells, myelocytes one normoblast marked anisocytosis and poikilocytosis hematocrit 10 8 per cent total proteins 4 6 per cent Sternal marrow puncture 38 per cent myeloblasts The administration of liver extract was followed by a dramatic response of reticulocytes to 30 per cent On discharge the hemoglobin was 60 per cent total proteins 6 1 Gm per cent

In spite of the severe suppurative intra abdominal complications which accompany walled off perforations in ileitis, pylephlebitis and multiple liver abscesses are rarely seen The report of Snavely is the only one to be found in the literature a colored male suffered with diarrhea, high fever ascites was probably present On one occasion only, cysts of amoeba histolytica had been found At examination, regional ileitis involving 5 feet of ileum was noted, a

fistulous communication between terminal ileum and the sigmoid was present, as also were pylephlebitis and multiple small liver abscesses No such complication of ileitis is seen in this series probably for the reason that almost all cases are instances of granulomatous rather than of suppurative disease Warren and Sommers quote an additional case in a Negress in which autopsy disclosed thrombosis of the inferior vena cava and external iliac veins following upon intestinal obstruction and complicated by numerous internal intestinal fistulas Intussusception is not mentioned in the literature as a complication of ileitis

Gynecologic Manifestations

There is little disturbance of endocrine function in the female as a result of ileitis Menstruation is not affected even in the severe cases This is in contrast to ulcerative colitis in which amenorrhea is a frequent manifestation of the severe and toxic phase of the disease, the return of the menses usually indicates the improved prognosis and the beginning of a remission

Fertility is unaffected by ileitis, pregnancy having been noted frequently in this series particularly during the remissions The relationship of pregnancy to ileitis may be represented in table 9

TABLE 9—*Relationship of Ileitis and Pregnancy*

Onset of Ileitis during Pregnancy	1 case
Onset of Ileitis after child birth	
(a) immediately	1 case
(b) two months	cases
(c) eight months	1 case
(d) three years	1 case
Ileitis pregnancy still births ([illegible])	cases
Ileitis successful surgical cure subsequent uneventful pregnancy and normal child birth	[illegible] cases

It is interesting to observe that one of these patients had two healthy babies after a successful short circuiting operation for ileitis (ileo transverse colostomy) It is noteworthy that a recto vaginal fistula which had been previously surgically resected in this case remained closed in spite of the two deliveries

The ileitis case seems to tolerate pregnancy much better than do those mothers suffering from ulcerative colitis. In colitis, the pregnancy itself is uneventful and the diarrhea and active symptoms of the disease are likely to undergo a remission. But a most active and severe recurrence of all the symptoms is likely to recur within a few weeks after delivery. In contrast, we note in ileitis one case in which the disease was observed in its initial phase during pregnancy followed by normal delivery, 3 cases with successful delivery, the mothers remaining well thereafter (table 9). Five cases are further seen *in which the ileitis recurred* after the birth of the child; in some of them the recurrence occurred so late thereafter that there is little reason to attribute the recurrence of the disease to the past pregnancy or parturition. Babson cited a case of terminal ileitis with obstruction and with an abscess complicating the pregnancy and resulting in abortion. Quite recently Raffensberger described the case of a 22 year old woman upon whom previously a short circuiting procedure had been performed for a regional ileitis. She remained well and free of symptoms even during an uneventful pregnancy which, unfortunately, terminated in a premature delivery of a stillborn child. A few days later, severe diarrhea and abdominal pain occurred, caused as demonstrated radiographically by an acute recurrence of the ileitis in the loop proximal to the previous anastomosis. Wilson, Gruman and Ashburn mention profuse vaginal discharge in one case; after resection of the terminal ileum the vaginal discharge ceased almost at once; possibly a fistula to the uterine cavity or vagina had existed. In one case observed a right salpingitis occurred as a result of the fistulous tract leading from the terminal ileum to the right fallopian tube. In another case the fistulous tract from the terminal ileum ended in the vault of the vagina, constituting a profuse suppurative open fistula successfully repaired by surgical intervention (personal communication, Dr. Ralph Colp).

8 Roentgenographic Study of Regional Ileitis

THE LITERATURE on the radiographic recognition of terminal ileitis more or less recognizes the classic description by Kantor of the "string sign" as the characteristic manifestation of the disease Not only was it the first radiologic study of ileitis, but, by its descriptive accuracy and terse and apt nomenclature, it has gained general and permanent acceptance Crane had previously used the word "string sign" to designate the attenuated thinned out segments of colon identified in spastic or irritable bowel The word and the description were so apt that Kantor borrowed the name to apply it to the similar appearance which occurred in the ileum in terminal ileitis

The string sign is a "thin irregular linear shadow suggesting a cotton string in appearance, and extending more or less continuously from the region of the last visualized loop of ileum through the entire extent of the filling defect and ending at the ileo cecal valves" (figs 27–30)

The explanation of the string sign" is to be found in the study of an opened specimen of old chronic terminal ileitis The thickening of the walls of the gut by inflammation and scar tissue infiltration encroach upon the lumen to narrow it the parallel process of cicatrization contracts or shrinks down the walls further to diminish the circumference of the intestine If the normal proximal lumen is 6 cm in diameter that of the diseased terminal ileum may be 0 7 to 1 0 or 1 2 cm in diameter throughout the area

indicated by the string sign Reconstruct such a specimen, as has been done, fill it with barium and take a roentgen film and the string sign is fully reproduced (figs 31–34)

Besides the "string sign" one observes in radiography



Figs 27 28 29 30 —Various Types of Terminal Ileitis with Characteristic String Sign Formations

Fig 27

of ileitis an indentation on the inner wall of the cecum at the insertion of the ileo cecal valve This indentation is regarded as due to the edema and inflammatory swelling of the terminal segment of ileum just at its approach to or abutment upon the inner surface of the valve of Bauhin

The cecum itself may be consistently spastic and irregular and frequently will be seen to be conical or persistently pointed in its shape This appearance often suggests an amebic granuloma of the cecum, a frequent site for ame-



Fig 28—(See Fig 27)

biasis implantation Strombeck in acute ileitis, noted pronounced swelling of the valve of Bauhin, the two lips of which may be conical and may bulge into the cecum He further claims that he was able to identify elongated ulcers 1–2 cm in the long axis and somewhat rounded ulcers along the attachment of the mesentery these ulcers occurring exactly at the point of passage of the intestinal vessels

through the muscularis A soft shadow in the mucosal relief can often be observed at the site of an abscess

In the upper ileum proximal to the diseased terminal segment ileitis produces alternate areas of constriction and dilatations corresponding to pathologic "skip lesions" and to "skipped areas," of normal mucosa The dilatation



Fig 9—(See Fig 27)

represents areas of normal mucosa lying between the constricted diseased skip lesions of inflammatory disease This disturbance of pattern may be followed upward through the ileum in advanced cases and even into the jejunum

It must not be presumed that the "string sign" of ileitis is present in all cases In many instances, only a distorted mucosal pattern of the terminal ileum may be noted (Last) (fig 35) The normal folds of ileum run

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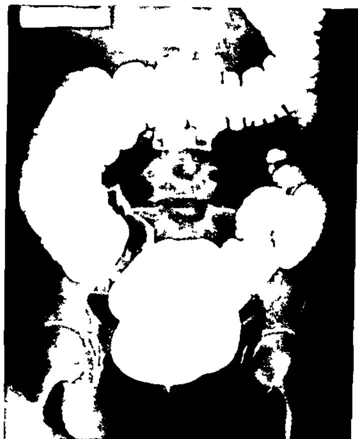


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students disarrangements of the mucosal relief that were very similar to those produced by mild disease or deficiency states Since this distortion is often difficult to read and to translate, the purely radiologic diagnosis must rely upon



Fig 31 [illegible] 34—Various Types of Regional Ileitis Involving one and two Loops of Distal Ileum Disturbed mucosal pattern tendency to polypoid formation indication of more extensive string sign
Fig 31

concomitant clinical facts Kirklin in a discussion of a paper by Brown, emphasized this point he says that shortening and rigidity of the segment and the string sign are late manifestations of the disease The earlier diag

longitudinally and parallel crossed by the markings of the transverse folds of the intestine, thus, a fine network of mucosal folds are normally visible When the area is in early stage of disease, when edema and active inflammation



Fig 30—(See Fig 27)

is taking place, but before cicatricial narrowing has intervened, the so called 'mucosal type,' the distortion of the mucosal pattern is the only radiographic sign that may be interpretable and acceptable (fig 36) Ruffin et al warn against interpreting slight changes in the mucosal arrangement as being due to disease or to deficiency patterns They were able to note, in control observations upon normal

above and below the lesion show relative hypomotility and delay, the serosal changes may be minimal Weber further warns against misinterpretation of the x rays because of wide variability of the normal mucosal pattern



Fig 33 —(See Fig 32)

The examination demands close scrutiny of each individual segment by multiple roentgenoscopic observations of the descending opaque meal and of the terminal ileum after it has been distended by the reflux of the opaque enema

In many cases radiologic evidence of ileitis is completely missing and yet the clinical data are so convincing that the diagnosis must be adhered to in the absence of confirmatory

nosis must be based upon inner changes in the relief pattern of the mucosa, a sense of diminished pliability and motility and local or general intestinal hypermotility. The greater the deformity the older and more advanced the lesion.



Fig. 32.—(See Fig. 31.)

Weber describes the radiologic picture of the early relatively unpronounced degree of submucosal infiltration as a flattening of the normally high mucosal relief pattern. If ulceration has taken place the relief pattern is jagged and irregular, not smooth and flat. In the advanced stages, the affected segment of intestine is shortened, its lumen narrowed, motility and pliability are lost. The affected segment shows relative hypermotility, the unaffected loops

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originating from the wall of the ileum, frequently trending downward toward the pelvis or toward the urinary bladder (fig 18) These appear like small spikes, only an occasional one traverses large distance to form a true elongated fistula

The upper "skip lesions" of disease and skipped areas of healthy bowel are usually easily picked out on the films



Fig 35.—Characteristic Disturbance of Mucosal Pattern in Terminal Ileitis Courtesy of Dr Franz Lust

It is remarkable how accurate reading of such films corresponds to the reality of the resected specimen One can ascertain almost to the inch the extent of the lesion as expressed in the x ray films and as confirmed at the operating table

Involvement of the cecum or of the other segments of colon is similarly to be sought after since combined instances of ileitis and colitis are not uncommon

roentgen signs (Yunich and Crohn) The "string sign" is almost pathognomonic, is always highly suggestive, on the other hand, the absence of all roentgenographic evidence does not in any manner preclude a positive diagnosis of ileitis



Fig 34—(See Fig 33)

In a very careful scrutiny of films it is often possible to discern evidences of fistula formation These fistulas appear as fine lines, attenuated skeins traversing from terminal ileum, to cecum or to transverse colon to sigmoid or to pelvic colon These lines may be seen only on fine study but should always be sought With a magnifying glass it is often possible to see several small potential fistulas

of filling the proximal part of the intestine with a substance which will pass through the partially obstructed lumen with difficulty." The radiography of the colon being negative, insufficiency of the ileo-cecal valve occurs in a sufficient majority of instances (probably 80 per cent) to allow regurgitation of the barium clysma into the terminal loop of ileum. By this means the string sign or irregularity of the mucosal pattern in the terminal ileum is usually visible. Unfortunately, in a fair percentage of cases, redundant loops of colon or of a pelvic colon with a long mesentery may overlie the terminal ileum to becloud or eclipse the visualization of that segment. For that reason the barium enema must often be supplemented by the barium meal. The barium meal offers the additional opportunity of observing the upper ileum and jejunum and allows for a better visualization of sinus and fistula tracts before the overloaded and redundant colon fills and obstructs the reading of the finer structures. The barium meal, consisting of 4 ounces of barium in a flavored water vehicle, must be followed hour by hour in its course through the jejunum and the ileum, particular attention being given to that phase when the terminal ileum is filling or is filled with the opaque mixture. The films are taken at the optimum time as determined by fluoroscopy. The mistakes and the omissions of diagnosis are often due to the arbitrary standards for plate taking and timing as set in some laboratories. Those technics that call arbitrarily for 3, 6 and 9 hour plates are likely to miss the optimum time for visualization of the terminal ileum. The terminal ileum may fill best in 3 hours or in 5 hours or 8 or 12 hours depending on conditions of individual intestinal motility; in cases with obstruction the delay may be long but the ultimate satisfaction in visualizing the disease in the terminal ileum will be rewarding. The barium meal further identifies the higher skip lesions and skipped areas, the dilated proximal segments of small bowel indicating more distal obstruction of the lumen of the bowel. It affords the basis for the

The Technic of Radiography

The string sign can usually be demonstrated equally well by the barium enema and by the barium meal. The first preference in working up a case is for the barium enema since this method delimits the colon, indicates whether universal or segmental colitis is present or absent, it is

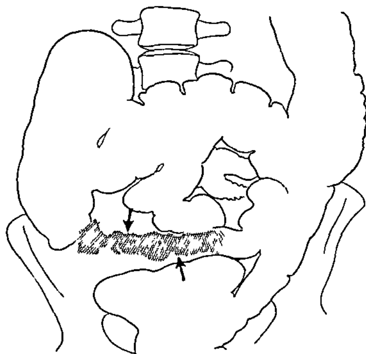


Fig 36—Terminal Ileitis Mucosal Type Note absence of the string sign irregular crenated margin of ileum disturbance of mucosal pattern

most important in a case of diarrhea primarily to eliminate the probability of ulcerative colitis diverticulitis or of neoplasm. Weber shows a distinct preference for the barium enema as the initial procedure in the radiologic diagnosis of ileitis. With the contrast enema the coils of the ileum are well elevated out of the pelvis, are distended and are readily manipulated under roentgenoscopic control by palpation through the abdominal wall. Furthermore, one must not overlook the danger

The string sign so characteristic of ileitis may be simulated by other diseases. Hyperplastic ileo cecal tuberculosis or ileal tuberculosis, primary or secondary may imitate the string sign as observed by Stierlin and Chaoul and more recently accentuated by Taylor. Connell has noted the



Fig 37—Demonstration of Barium Iced Saline Method for Early Visualization of the Intestinal Tract (Courtesy of Weintraub and Williams)

string sign to be present consistently in ileo cecal tuberculosis. He notes irregularity of the shadow in the terminal ileum and conical contraction of the cecum. The ileo cecal valve is visible to an exaggerated degree. The lips are gaping through the valve and occasional obstruction at this point may occur. The additional involvement of the cecum more likely invites the diagnosis of tuberculosis

differential diagnosis of regional ileitis and jejunitis from the somewhat similar and easily confused picture of sprue, of vitamin deficiency manifestations, of intestinal Hodgkin's disease or of lymphosarcoma It allows further for the minute study of distal fistula formation from loop to loop of small or of large bowel

The novel suggestion of Weintraub and Williams of administering the barium meal followed soon thereafter by the drinking of an iced saline solution affords a rapid and simplified means of quickly filling the distal loops of the small bowel The barium meal is very promptly propelled by peristaltic activity so that within a half hour almost all of the loops of jejunum and ileum are fully visualized Even the mucosal pattern of the distal loops are well defined Of 235 normal control cases, in 190 the head of the barium saline meal had reached the cecum in one half hour or less The mucosal pattern was in all cases as good as that obtained on routine small bowel examination, especially in the terminal ileum If the method of Weintraub is proven to be free of faults, and artefacts are not created by the rapid propulsion of the barium the newer technic may materially simplify and accelerate the radiographic recognition of diseased distal areas of intestinal involvement (fig 37)

Oral intubation of the small intestine by means of a duodenal tube or a Miller Abbott tube, has been employed by some authors The tube or balloon is passed to the required depth as determined by fluoroscopy, then barium suspension is injected through the tube to the probable site of the disease This allows for intimate and exact study of a localized segment of intestine free from the overlying shadows of extraneous loops of bowel The method is good and rewarding though its use is not very universal Actually the barium meal is so successful when properly administered and interpreted that the more devious and difficult and time consuming method of intestinal intubation is rarely called upon or utilized

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9 The Diagnosis of Regional Ileitis

THE DIAGNOSIS of regional ileitis is essentially a clinical one, based upon the characteristic subjective symptoms and the physical findings. The x-ray diagnosis is valuable as confirmatory evidence and allows for anatomic interpretation of the lesion. It is a grave error to think of ileitis as an obscure disease difficult or impossible of diagnosis. Ileitis has clear-cut subjective and physical features, which when combined spell out a succinct clinical diagnosis. The combination of diarrhea, fever, anemia and fistulas, internal or external, with or without an abdominal mass, with or without radiographic confirmation means a possible or a probable diagnosis of ileitis. The negative sigmoidoscopy rules out the usual case of ulcerative colitis, 95 per cent of which cases give a distinct pathologic sigmoidoscopic picture. The remaining possibility is a right-sided segmental colitis, to be differentiated from regional ileitis. Segmental colitis may have and does have anal complications and rectal fistulas but has no fistulas to the abdominal wall and no internal fistulas or intra-abdominal masses.

To recapitulate the diagnostic significance of the symptoms and signs of ileitis:

The diarrhea is the most common feature; it may be absent in 15 per cent of the cases.

Fever is frequent and significant, but the majority of the long-standing low-grade cases are afebrile.

Anemia may be so moderate as to be insignificant; a hemoglobin reading below 65–70 per cent is of value

but not necessarily so since combined ileitis and colitis or ileo colitis of a nonspecific granulomatous type must be also considered

Carcinoid tumors of the terminal ileum, endometriosis with implantations on the serosal surface of the ileum and occasionally benign new growths within the lumen of the ileum may stimulate the string sign of ileitis particularly when obstructive phenomena are also present In rare instances, small round transparencies within the barium filled small intestine indicate the presence of polyps, these are the accompanying manifestations of ileitis, just as they indicate in ulcerative colitis an advanced stage of inflammatory reaction with secondary polyposis In cases of ileitis with mass formation the loops of upper ileum may be displaced laterally by the mass leaving a void area corresponding to the inflammatory tumor formation

Rosenberg mentions enterogenous cysts at the ileo cecal junction as simulating the roentgen picture of terminal ileitis

The positive roentgenographic evidences of ileitis are usually present in a well defined clinical case However, it must always be remembered that all confirmatory roentgenologic evidence may be missing in a subsequently clinically proven case the roentgen limitations in atypical or early ileitis become self evident with increasing experience (Yunich and Crohn)

culous pathogenicity In a recent survey of anal fistulas, summarizing 600 cases, Jackman and Buie found 87 8 per cent negative for tuberculosis In the true tuberculous fistulas, primary affects elsewhere in the body, usually the lung, were always demonstrable This reversal in the view point of the relationship of tuberculosis to anal fistulas is due in large part to the increasing role which ileitis and colitis play as etiologic factors in the incidence of such perirectal complications

It is particularly important to have sufficient mental fortitude to sustain the diagnosis of at least probable ileitis, even though many significant clinical features are missing and the x ray diagnosis is negative On several occasions one has been saved from a blatant error by including in the provisional negative diagnosis at least the possibility of ileitis The following experience is illustrative

The case was reported as nervous diarrhea, irritable colon, but the proviso was added of a possible ileitis Five years later the symptoms flared up and now exploratory laparotomy showed regional ileitis with an ileo sigmoid fistula Not that every case of diarrhea should be classed as a possible ileitis, but the association of diarrhea with a fistula a mass, fever, or anemia any such combination calls for diagnostic caution and acuity

The low grade fever of regional ileitis is often overlooked by general internists who are likely to pay little attention to mild diarrhea, or to the complaints of occasional faint abdominal pain The patient may not consider two or three loose bowel movements as diarrhea the abdominal pain may be minimal and no positive physical signs may be discoverable These cases of ileitis with low grade fever are usually confused with brucellosis or undulant fever particularly when a low titer agglutination against the Melitensis organism has been reported Many a case of ileitis has been overlooked because of a positive agglutination of 1 40 or 1 80 against brucella One such case was

Loss of weight is significant but may not be extensive An abdominal mass may be present, but most frequently is absent

Fistulas, internal, external and perirectal are the most nearly pathognomonic manifestations of the disease, particularly when associated with diarrhea and with the other positive signs and findings of ileitis

The radiographic study is exceedingly important when positive, a negative finding does not necessarily nullify a clinical tentative diagnosis of ileitis Any one symptom, especially any combination of two or more of these signs and symptoms should suggest the consideration of ileitis Diarrhea alone, diarrhea plus fever, diarrhea with fistulas, an abdominal mass with fever, an intestinal or perirectal fistula, any combination of such symptoms and physical findings is suggestive An illustrative case in point is worth quoting because of its significance

P B (Serial No 197) Male age 39 years For many years he had suffered with mild diarrhea Eight years ago he had been operated upon for a rectal fistula Subsequently he had lost [illegible] pounds of weight complained of abdominal cramps and persistent diarrheal movement The physical examination was negative except for slight tenderness over the cecal area of the abdomen and suggestive clubbing of the fingers The rectal and sigmoidoscopic examination were negative The radiographic examination barium enema and barium meal were reported as negative except for some evidence of a spastic colon The terminal ileum was well visualized appears somewhat irritable in its distal portion but fills well and is distensible The report to the referring physician stated that although the diarrhea fever and the past rectal fistula strongly suggested ileitis the absence of confirmatory radiographic evidence made such a positive diagnosis impossible It was urged that the patient be carefully observed for future development Six months later the patient developed a fistula from the ileum to the *sigmoid* At operation a regional ileitis was discovered involving [illegible] feet of ileum proximal to the ileocecal valve An ileotransverse colostomy with transection of the ileum resulted in cure

The significance of the perianal fistulas cannot be overlooked In former years such fistulas were regularly regarded as either being tuberculous in nature or were suspected of a tuberculous origin Mummery in 192[illegible] regarded at least 15–20 per cent of perirectal fistulas as of tuber

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even published in medical literature in this country (Sproull) as a case of undulant fever with unusual intestinal changes, this, before the first description of ileitis as a clinical entity. Years later, exploratory operation and resection of the ileum revealed the true nature of the disease as one of ileitis with low grade fever, the doubtful low grade agglutination titer against brucella having only confused the diagnostic issue.

Ileitis which presents itself as a case of continuous low grade fever, with low leukocyte count, with occasional joint involvement, clubbing of fingers or eye complications, particularly when a heart murmur is present, is likely to be overlooked, particularly when the minimal diarrhea, which is the actual key to the diagnosis, is ignored. All of these manifestations of a generalized disease are common to both ulcerative colitis and to ileitis; omit the diarrhea and the general symptoms resemble brucellosis, rheumatic fever, subacute bacterial endocarditis, lupus erythematosis disseminatus or Libman-Sachs disease. Rosenblate, Goldsmith and Strauss cite a case of regional ileitis unrecognized for four years, during which time, because of a soft systolic mitral murmur over the precordium, the case had been considered as one of chronic heart disease or subacute bacterial endocarditis, in spite of repeated negative blood cultures. Sprague et al. report a case of long standing fever in a girl of 15 years of age who presented the clinical picture of an irregular fever with temperatures ranging between 101 and 104 F. with polyarticular rheumatic-like arthritic manifestations and perirectal abscesses, the whole clinical picture being due to a regional ileo-colitis.

The significance of the cardiac murmur may be over-emphasized. At least 5 cases in this series had had rheumatic fever and bore residual systolic mitral or aortic murmurs. Add to the old rheumatic cardiac murmur a low grade fever and the possibility of ileitis or segmental colitis is rarely *considered. This is all the more important* because in one case in this series an acute endocarditis

actually occurred as a complication while the patient was under observation A young woman with recognized regional ileitis was under observation preparatory to operation. An increased degree of fever was associated with the development of a systolic murmur at the cardiac apex the murmur was heard with daily increasing intensity, a low rough murmur was audible and was transmitted to the mitral area A blood culture was negative at the height of the fever Penicillin was instituted, the fever subsided in seven days and the cardiac murmur ceased to be audible The patient was later successfully operated upon for regional ileitis No further cardiac manifestations occurred

The larger and sometimes the smaller joints of the hands or feet may be implicated in diarrheal diseases, the so called "arthritis dysenterique," but the significance of the arthritis as an intestinal manifestation is usually overlooked in favor of a diagnosis of rheumatic fever with joint involvement

The mild or moderate eosinophilia that frequently accompanies ileitis and colitis may suggest and be confused with periarteritis nodosa

The eye complications which occur occasionally in ileitis but more commonly in ulcerative colitis again are usually overlooked and are classified in the tuberculous or rheumatic category (Sprague et al) Ophthalmologists of wide experience are conscious of the fact that inflammatory lesions of the eyes are not uncommon complications of intestinal diseases Iritis iridocyclitis, keratitis corneal ulceration phlyctenular conjunctivitis all constitute focal manifestations of intestinal diseases

Differential Diagnosis

When a suggestive "string sign" is present, or when a disarrangement of the pattern of the intestinal mucosa is noticeable in the roentgenograms various other possible intra abdominal diseases come into consideration in the differential diagnosis When the upper ileum and the

jejunum show puddling and segmental delays and disturbed mucosal patterns, sprue and the vitamin deficiency diseases deserve close notice Here the differentiation between sprue and ileo jejunitis is often difficult (fig 38)

Intra abdominal Hodgkin's disease by its fever and low leukocyte count and its possible intestinal involvement may



Fig 38—Diffuse Ileitis Whole Ileum Involved Scattered skip lesions fistulous tract in lower ileum between loops of small bowel constipation Patient preserved his well being

simulate ileitis Multicentric intestinal lymphosarcoma with its characteristic areas of intestinal dilatation, with hemorrhage fever and perforation and rapid wasting may be confused with ileitis Both Hodgkin's disease and intestinal sarcomatosis are intensely malignant and progressive diseases with early fatal issue in contrast to the more mild and low grade continuous course of chronic regional ileitis

The "string sign" of the terminal ileum may be simulated by (figs 39 and 40) hyperplastic ileo cecal tuberculosis, carcinoid of the terminal ileum, endometriosis of the terminal ileum, enterogenous cysts about the terminal ileum, actinomycosis, intestinal



Fig 39 — Amebic Dysentery Characteristic Deformity of the Cecum Incomplete Filling of Terminal Ileum This radiograph is almost identical with that seen in nonspecific granulomatous ileo-colitis

Primary intestinal tuberculosis as a manifestation of bovine infection is exceedingly rare in a complete survey of all the postmortem and surgical pathologic material at the Mount Sinai Hospital over the last fifteen years, only 4 cases of primary intestinal tuberculosis survived a critical analysis (Crohn and Yarnis) In 2 of the these cases,

the ileum alone was the site of typical miliary tuberculosis, tubercle bacilli were found in the sections of the histologic studies All other cases were those of ileo cecal or ileal tuberculosis secondary to open lesions in the pulmonary areas with caseating cavity formation and positive sputum or positive gastric residue findings for tubercle bacilli



Fig 40—Appearance of Appendix Filled with Barium Resembling String Sign of Ileitis

Cases of regional ileitis regularly have negative chest findings by physical examination and by radiographic study Cases of secondary intestinal tuberculosis have strongly positive chest plates with evidence of cavity formation and with positive sputum findings That intestinal tuberculosis can simulate exactly the string sign of ileitis has been amply demonstrated (Crohn and Yarnis) This point has again been recently emphasized by Connell Blackburn

found the Mantoux Test negative in 19 of the 22 cases and x-rays of the chest uniformly negative in regional ileitis.

Argentaphilic carcinoid tumors infiltrating along the mucosa of the terminal ileum represent a favorite site for that lesion and can simulate the clinical picture and the radiographic string sign of ileitis. In one case in my experience, the terminal ileum was resected under the supposition that it represented a case of ileitis; the gross specimen was passed from hand to hand and was accepted as one of ileitis by many long experienced in handling such surgically resected specimens. Only on histologic study was the true character of the lesion identified as one of carcinoid tumors of the terminal ileum with metastases to the mesenteric lymph nodes.

Up to 1939, 237 cases of argentaffine tumors of the small intestine had been reported in the literature; obstruction occurred in 24.4 per cent of these. Pennington and Priestly report a case of carcinoid tumors of the terminal portion of the ileum invading the mesentery. The abdominal mass involved several loops of the terminal segments of the ileum. The lesion was malignant, several metastatic tumors being present in the liver. McLeod adds 2 cases to 283 reports in the literature (1944); intestinal obstruction in the terminal ileum and organ metastases were commonly observed. Dockerty and Ashburn in a review of the literature describe carcinoid tumors (so called) of the ileum. They detail 30 cases of carcinoid of the terminal ileum, 18 of which had metastasized locally or distally. Small orange submucosal nodules were arranged linearly with a minimal degree of ulceration. Regional lymph nodes were involved in 11 cases; in 5 metastases to the liver were present, suggesting a low-grade type of carcinoma virulence.

Endometrial transplants on the serosa of the terminal ileum with or without invasion of the intestinal walls occasionally may be confused with ileitis; the string sign is almost identical. The intestinal bleeding with the menses may, if present, suggest the true nature of the lesion. A

case of endometriosis as a cause of intestinal obstruction has been described (McGuff et al), in which the segment 5 cm proximal to the ileo cecal valve was involved by endometrial transplants The clinical picture resembled in general a case of regional ileitis with intestinal obstruction

Enterogenous cysts about the ileo cecal angle are exceedingly rare, but may simulate roentgenographically the constriction of terminal ileitis (Rosenberg)

Actinomycosis, intestinal, with abdominal wall fistulas may simulate ileitis the finding of the characteristic ray fungus in the discharges from the fistula will save much confusion and often embarrassment The possible confusion between ileitis and sarcoidosis has already been discussed (page 16) Sarcoidosis of Boeck involving the small intestine as a granulomatous lesion was described recently by Watson and his associates the identity of ileitis and sarcoidosis was even suggested by Hadfield Snapper has, however, made the point that he has never encountered a case of sarcoidosis with a lesion of the intestine, nor have his many cases of ileitis ever shown sarcoidosis Blackburn states that in ileitis there is no record of swelling of the fingers and toes lymph adenopathy or the "uveo parotid syndrome such as is observed in typical sarcoidosis Sarcoidosis is a generalized disease affecting the reticulo endothelial structural system Intestinal involvement by sarcoidosis without generalized implication of other organs would be difficult to accept

10 Considerations Regarding Therapy in Regional Ileitis

IT IS AN OPEN QUESTION whether any conservative or expectant form of medical treatment is warrantable in regional ileitis. True, it has been shown that in this series *twelve out of 222 cases progressed to what seemed* to be spontaneous resolution with the disappearance of roentgen evidence of the disease. True too, that it has been demonstrated that in a percentage of cases the lesion remains in the terminal ileum showing over the course of years little tendency to extend in an oral direction. These cases develop cicatricial stenosis, the true "string sign" in roentgen study, and some of them eventually progress to intestinal obstruction. They may remain stationary without developing skip lesions year after year. Occasionally abdominal wall fistulas have been demonstrated to have closed spontaneously. Thus there would seem to be some rationale for the development of a conservative form of medical therapy.

On the other hand in the usual case of regional ileitis when first seen for diagnosis advanced skip lesions higher up in the ileum can often be demonstrated proximal to the parent distal area of involvement. And many if not most of the cases show over the course of years not only proximal intestinal extension but if conservatively observed, demonstrate a continuity of clinical symptoms that bespeak a dynamic disease having an active life cycle. If not stayed by surgery the repetitive series of fever, diarrhea, anemia

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in this series have either been operated upon or are awaiting a decision for surgical intervention, because of the progression of symptoms and the appearance of complications

Since the definitive method of handling recurrences after operation has not yet been determined, these cases, too while being observed, must have some plan of conservative therapy

The indications for conservative medical therapy should apply to

1 Those cases who refuse surgical intervention and insist on palliation

2 Cases of long standing low grade intensity whose pathologic lesions show no tendency to progression

3 Postoperative recurrences whose future course of treatment has not yet been determined

For all other cases, constituting the largest group surgical intervention seems indicated as soon as the diagnosis has been established

Diet

A bland low fat protein rich diet should be instituted Abundant proteins and the liberal use of carbohydrates are necessary to maintain nutrition against the wasting of the disease and against the hypoproteinemia that may ensue as a result of protracted fever and diarrhea Coarse fruits and vegetables should be eliminated soft vegetables well cooked should be pureed or passed through a collander Fruit juice may be allowed in limited quantity soft fruits such as bananas apple sauce soft pears, ripe peaches are allowable The greatest attention is paid to meats and fishes cheeses protein milk and eggs as foods with high nitrogen content The diet should be supplemented by the administration of protein or casein hydrolysate with high amino acid content 6 8 or 12 ounces a day taken in milk water fruit juices cocoa substitutes or in any manner that makes them possibly palatable to taste

and fistulas *indicate a pathologic process that, by itself,* suggests no cessation of the underlying infection. It is in this latter type of case that delayed surgical intervention is so often disappointing and probably accounts for the high percentage of recurrences after operation.

If one could determine, by study of a case over a course of years, that a particular patient had a stationary type of lesion which did not show progression, one might be warranted in attempting some form of conservative therapy. By that same token, if the patient were one whose lesion showed progression, then medical therapy should be rapidly *replaced by surgical intervention. But would the delay,* protracted over a course of several months if not years, be warrantable? And are not the surgical failures to be charged up against procrastination when only too late one becomes conscious of complications, sequelae and progression of the lesion? Clark and Dixon have stated that anyone who has seen the irremediable damage sustained by an affected segment through prolonged delay must realize that there is no known medical treatment that will dissolve a fibrotic stenosis, or will close a fistula that develops in the later stages of ileitis. Lahey and Sanderson make the *categorical statement that there is no medical treatment* worth consideration in regional ileitis.

The percentage of spontaneous cures in this present series was small, actually 5.4 per cent. The percentage of surgical cures is high, even when reckoned conservatively, and is grossly well over 80 per cent. Then why contemplate palliative treatment at all, why not operate as soon as the diagnosis has been established? These twelve cases of spontaneous healing represent those who have refused operation and preferred to undergo expectant therapy. They are the small minority who have won out by their own per*sistence.* But it is questionable whether the success in this minimal group can be utilized to formulate a plan of expectancy treatment that will largely apply to the massed group of cases. The remainder of the group of 210 cases

6 30 p.m. *Dinner*
Choice of soup
Choice of main dish Lean beef (boil broil or roast) chicken turkey or fish Portion of strained cooked vegetable Portion of potato, rice or spaghetti Bread or roll with butter or jelly Dessert Jello cornstarch pudding or apple sauce Milk cocoa or weak tea.
9 30 p m
Milk soft drinks may be taken in small quantities if not too cold and most of fizz is expelled (or see 10 30 and 3 30)

Diet

Foods Allowed in Diarrhea

All food should have their roughage reduced to a smooth form by putting through a sieve so that no rough indigestible portions are left to irritate the bowel

Milk At least a pint a day Milk need not be boiled Cultured milks may be used acidophilus buttermilk, etc Mellin's food or malted milk may be added to milk

Note Most persons tolerate milk very well However, milk may cause diarrhea in those few persons who are 'allergic' to milk Those who find themselves "allergic" to milk (diarrhea) should omit it

Eggs Two or three daily Use in any form except raw or soft boiled

Cheese Any mild cheese may be used cottage pot or sour cream cheese gruyere swiss, etc Small portions of sour cream

Cereals All highly milled grains that are well cooked farina cream of wheat, wheatina, cornmeal white rice, ralston, etc

Note When using ready to serve cereals, check advertising and reject all cereals containing *bran* Safe ready to serve cereals are cerevim cornflakes grapenut flakes pablum puffed rice, puffed wheat Spaghetti noodles and macaroni in moderation

Meats All lean meats boiled baked or broiled ground lean steak roast beef steak liver of all kinds veal, lamb, smoked ham chicken squabs turkey

Fish All white fish boiled baked or broiled halibut cod, flounder, sea bass etc shell fish oysters and clams

In one case of high ileo jejunitis where operation was contraindicated, a gain of 50 pounds of weight and a return to fair health and strength followed a conscientious forced attempt at superalimentation with protein foods and amino acid commercial preparations

Conservative Palliative Treatment of Regional Ileitis

General Directions

Live in an atmosphere which is peaceful Try to control anxiety, worry or mental upset Plan every day so as to have a rest period and as much quiet as possible

Fresh air and *sunshine are fine aids to a quick recovery*

No competitive games or strenuous exercises Plan recreation which does not produce nervous tension or great fatigue, no tennis match, no card games for money, no horse back riding

Have a full and highly nutritious diet by eating three meals with light mid morning, mid afternoon and evening lunch That is, eat once every two and a half hours throughout the day and little or nothing after 10 P M The diet which is suggested for diarrheal diseases is as follows

Sample Menu

8 00 a m *Breakfast*
Orange or tomato juice ¼ cup (dilute with water if liked better) Cereal with milk and sugar Bread (white) 2 slices (toasted) with butter Egg (1 or 2) boiled hard poached shirred or scrambled Milk cocoa or weak tea (1 cup)

10 30 a m
Hard boiled egg and cracker and milk cocoa or weak tea and cracker

1 00 p m *Lunch or Supper*
Choice of soup strained dried bean or split pea soup or cream soup (made with strained vegetables) or broth and any other strained soup
Choice of main dish Eggs or macaroni and cheese or portion of liver meat or fish
Serving of potatoes rice or noodles Bread (white) 2 slices with butter Dessert Strained cooked fruit plain cake or custard

3 30 p m
Banana or ¼ cup orange or tomato juice (or see 10 30 a m)

3 Avoid any gas forming food such as cabbage corn kohlrabi, broccoli, pickles and relishes of all kinds, also skins of baked apples and potatoes Eat no beans, peas or lentils except in pureed form

4 Avoid nuts raisins, coconuts, figs, dates, etc, even if used in small amounts in puddings or cookies

5 Avoid heavy fat foods gravies, sausages, pastries, doughnuts, fried meats and fish

6 All condiments, especially pepper, mustard horse radish, vinegar, etc are best avoided Therefore, do not use any highly seasoned and spiced foods, such as smoked meats and fish, frankfurters, most canned meats and fish, salt fish, olives, etc

7 Avoid fish high in fat—salmon, shad, etc and shell fish shrimp, lobster and crab

8 Avoid all grossly sweet foods preserves, most candies all rich cakes with icings and fillings

9 Alcohol is an irritant and should be avoided

10 Coffee should be omitted from diet, and tea served weak

11 Care must be taken not to use certain foods which are laxative as large amounts of lemon grapefruit or orange juice, raw vegetable juices, long iced drinks and many cups of too hot drinks as well as melons grapes, plums molasses raw or soft boiled eggs

Ambulation

Most cases of regional ileitis being afebrile, may be allowed some physical activity They are best treated as ambulant cases because the long course of the disease would make persistency in insisting upon bed rest a psychic and mental handicap Most of the patients suffering from ileitis are not strong enough to work or attend higher educational schools or colleges but they are happier up and about and would probably gain little by prolonged bed rest The acute cases and those with a febrile course should have bed rest during the active phase thereafter early ambulation is advisable to preserve muscle tone

Bread White bread (not too fresh), melba toast, zwieback, rolls, plain sweet breads like brioche, also all crackers made of white flour

Butter In moderation Thin sweet cream if well tolerated

Fruits With the exception of orange juice and ripe banana, all fruits must be cooked and sieved Note cooked dried fruit and canned fruit should likewise be sieved Use apples, pears, peaches, prunes, apricots, etc

Vegetables Use tomato juice Sweet or white potatoes cooked any way but fried Carrots, green peas, string beans, *onions, spinach, beets turnips, tomatoes, should be cooked* and pressed through a sieve In milder cases, cooked chopped spinach and beet tops asparagus tips and fresh tender lettuce may be used Note Canned infant foods are very satisfactory for use

Desserts Custards, Bavarian cream, blanc mange, bread, rice and tapioca puddings fruit whip, gelatin jellies plain, sponge and angel cake, plain cookies Ices and ice cream are not desirable but may be used in moderation in mild cases

Miscellaneous Strained jams and preserves may be used in limited amounts grape, pear apricot and pineapple juices may be used in small portions Juices of all mild cooked fruits may be used with added dextri maltose (not lactose which is laxative) *Hard candies are to be encouraged*

A certain amount of seasoning is allowable, that is, salt and pepper in moderation

Foods to Avoid During Diarrhea

1 Avoid all raw fruits and vegetables except strained orange juice in small amounts and ripe bananas All other fruits should be stewed

2 Avoid bran in (a) coarse breads (pumpernickel whole wheat breads, muffins health breads, etc) (b) coarse crackers (whole wheat, rye crisp swedish wafers, etc) (c) coarse cereals (oatmeal brown rice, barley, hominy petti-

some of the suppurative complications call for antibiotics that would tend to sterilize the bacterial content of the intestinal lumen Some efficacy of the sulfonamides in controlling the symptoms and progression of the disease seems suggested in studies of the use of sulfasuxidine and sulfathaladine (Crohn) in ileitis though convincing proof is lacking and though these drugs in the largest percentage of cases fail to accomplish any striking therapeutic result Sulfasuxidine (succinyl sulfathiazole) in doses of 0 25 grams per kilogram of weight is frequently employed the usual method is an initial dose of approximately 20 to 36 half gram tablets (10–18 grams) followed by dosage of five to nine tablets four times daily by oral administration Sulfathaladine (phthalyl sulfathiazole) 0 1 grams per kilo gram of weight usually 2 3 or 4 half gram tablets four times daily are equally efficient

Both of these drugs are bland and relatively free of untoward results Agranulocytosis has not been observed in this series nor has hepatitis been seen except in one instance Many patients have taken one or both drugs for protracted periods in one instance 3000 tablets were continuously imbibed over a course of six months without untoward results In many instances the disappearance of external abdominal wall fistulous tracts has been observed apparently as the result of sulfa therapy by oral adminis tration This is in itself a large accomplishment even though as a rule the insoluble sulfonamides do not control the active symptoms or the progression of the disease in regional ileitis [61]

Penicillin has no apparent specific effect on ileiti , though it is useful in controlling the suppurative complications when walled off perforation does occur As a preoperative and postoperative antibiotic form of therapy penicillin is in great favor with most surgeons Streptomycin too when given intramuscularly 2 grams daily in divided six hour doses, and one gram orally coincidentally, may sterilize the intestinal tract and produce a sterile culture of the

(Femoral phlebitis and pulmonary embolism have not been noted in my cases of this series)

Various Medications

In dehydration, particularly with diffuse draining fistulas, water and electrolyte replacement is best attained by the use of parenteral intravenous therapy Saline solution, Ringer's solution, 5 per cent glucose in water or in saline and the protein hydrolysates or amino acid preparations are indicated in amounts of 1500 cc per day, or 100 to 150 grams of protein daily Blood plasma and occasional transfusions of 500 cc are indicated for protein replacement and in instances of advanced anemia

In chronic ileitis vitamin replacement is strongly indicated Concentrates of vitamin B complex reinforced by thiamin 10 to 20 or more milligrams per day may be administered orally though the absorption in the face of diarrhea may be problematic In all cases, intramuscular injection of crude liver extract and of vitamin B complex, 2 cc of each, *should be given into the buttock every other day*, larger doses, as in sprue, may even be indicated It is rare that the other vitamins are indicated, there is no material deficit of vitamin A or carotene, nor of ascorbic acid nor of vitamin D in instances of ileitis since the diarrhea is rarely so profound as to create such vitamin deficiencies except after extensive and repeated surgical resections or short circuiting procedures Synthetic vitamin K is indicated, however, in all instances of hemorrhage from the bowel wall even though the prothrombin time is well within the normal range Five to ten milligrams of synthetic vitamin K daily intramuscularly, should as in ulcerative colitis, control the hemorrhagic manifestations

The insoluble sulfonamides are indicated in regional ileitis, even though the therapeutic result has not been convincingly demonstrated Whether the disease is bacterial *in origin* or nature has not been demonstrated But the bacterial contamination of the intestinal ulcerations and

11 Surgical Treatment of Chronic Regional Ileitis

THE SURGICAL RELIEF of regional ileitis is indeed a complicated and rapidly changing picture It should be interesting chronologically to follow the trends of opinion over the last fifteen years and to note the various schools of thought and of procedure For the subject is apparently still in a state of flux, as is natural where methods change procedures differ, judgments do not agree and the follow up period is all too short

In general, one may note historically certain salient or outstanding surgical procedures in the passing years of experience

1 Resection in one stage was the initial procedure of choice

2 The gradual evolution of a two stage procedure (short circuiting, followed subsequently by resection of the original lesion)

3 Adoption of a single stage operation, namely ileo transverse colostomy, with transection of the ileum, as a sufficient procedure to induce cure

4 Introduction of the Mikulicz technic, for primary resection by the Lahey Clinic

5 Persistence of the two stage operations favored by the Mayo group

6 Preference of Bockus for primary resection

7 Skepticism of some of the Boston surgeons for all types of procedures

feces, and yet it is questionable whether streptomycin has any clear indications for its use in the chronic protracted form of ileitis In the acute cases, and in the febrile forms, streptomycin may be pragmatically utilized though its effects have not yet been proven of clinical benefit I have actually seen one case in which streptomycin produced a sterile culture of the feces without in any way controlling the activity of the symptoms And yet, in a severe and febrile case its use experimentally could well be justified

Radiation therapy has been rather extensively employed, it was originally invoked by Eggers for the control of cases of intestinal granulomas and has been recommended and used by many writers in the literature My own experience with radiotherapy in ileitis has been very disappointing, though it has been limited to few cases We have had opportunity to observe the use of extensive radiotherapy in 18 cases, the radiation therapy having been previously employed by clinicians in attempts to control the disease and its complications Those cases that I have seen have all been failures, if there have been successes in the use of radiotherapy in ileitis they were not apparent in this series under study, nor when employed by me as an initial form of therapy

In instances of intestinal obstruction the Miller Abbott tube is beneficially employed and by decompressing the intestinal lumen rapidly produces amelioration of the obstructive phenomena

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8 Growing realization of the increasing incidence of recurrences following all types of surgical interference

1 The initial surgical procedure at Mount Sinai Hospital practiced by A A Berg was primary resection, as was carried out on the first 14 cases of terminal ileitis, this series was carried up to 32 instances of resection by Berg in 1936 Correspondingly, most of the early cases in the literature concerned themselves only with primary resections of the terminal ileum In 1936, Koster, reviewing 100 operated cases from the literature, found resection almost universally carried out as the procedure of choice, adding 17 cases of his own, most of which had been resected In 1939, Ravdin and Johnston, reviewing the surgical literature to date, found 290 instances of primary resection against only 88 instances of short circuiting procedures In 16 cases, enterostomy alone had been performed

2 Already in 1933 one notes the suggestion independently by Clute and by Homans and Hass of ileo transverse colostomy, that is, a short circuiting of the lesion as a sufficient procedure, rather than resection Unfortunately, neither contribution mentions whether transection of the ileum proximal to the lesion had been performed Even before this date, Estes and Holm had warned against such a procedure they demonstrated in 2 human cases and by animal experimentation that huge dilatation of the side tracked and excluded loop of ileum could and did occur This point of view however, was subsequently contradicted by the studies of Ginzburg Colp and Sussman By surgical experience, substantiated by careful roentgenologic studies, these latter authors proved that a short circuiting procedure with transection of the ileum was a safe and satisfactory procedure that involved no complications from the excluded loop of ileum

By 1934, some of the members of the Mayo group (Clark and Dixon) were already experimenting with short circuiting procedures, having utilized such a plan in 5 cases out of 13 operables Again, transection of the ileum was not

mentioned In 1939, Clark and Dixon suggested for the early stages of the disease a simple short circuiting procedure with transection of the ileum which carries a low mortality and provides an opportunity for the diseased segment of the bowel to improve by being placed at rest Subsequent resection of the diseased area was utilized if activity of the original site of disease continued If the disease process was far advanced primary resection, a radical extirpation of the diseased segment, was advocated

Mixter (1935) utilized a one stage or a multiple stage procedure in 11 cases, but unfortunately this small series carried a mortality of 4 cases or 36 per cent In 1936, Koster for the first time warns that if a short circuiting procedure is to be performed transection or "occlusion" of the ileum must be carried out he still preferred primary resection since he suspected the undesirability of leaving in situ the original focus of infection

The importance of transecting the ileum above the diseased segment was realized in the following case in this present series

Case H S (Serial No 146) Male age 21 years For eighteen months this young man had suffered with diarrhea fever and abdominal cramps A mass in the right lower abdominal quadrant had formed He had been operated upon at that time and a short circuiting procedure had been carried out without transection of the ileum Diarrhea persisted there was a weight loss of 50 pounds edema of the lower extremities was present due to hypoproteinemia Clubbing of the fingers and severe secondary anemia (hemoglobin 62 percent) were evident At operation a transection of the ileum above the persistent and residual ileitis was the only procedure performed This was followed by a regain of the 50 pounds of weight lost and a subsidence of the peripheral edema of the lower extremities Unfortunately two years later a recurrent ileitis proximal to the old anastomosis was capable of demonstration a two stage resection of the recurrent ileitis resulted in cure

3 The transition of the Mount Sinai group from primary one stage resection to two stage resection and finally to a short circuiting procedure only is interesting to observe In 1936, though primary resection seemed to be in favor it

was noted that both Lewisohn and Colp had 6 cases of short circuiting procedures with good results Lewisohn later reported (1938) 9 cases of short circuiting or two stage procedures with only one death He again strongly emphasized that a lateral anastomosis between upper healthy ileum and the colon, without transection of the ileum above the diseased segment is a useless operation since the affected part of the bowel is not put at rest

In the one fatal case, a primary ileo transverse colostomy with transection of the ileum had been primarily performed After a sufficient interval of what was then regarded as the proper sequence, the second operation of resection of the primary residual focus of disease was carried out The resected specimen was now fully healed and cicatrized Unfortunately, the child died postoperatively of pulmonary embolism due to an old rheumatic endocarditis The tragic death and the evidence that the secondary intestinal resection had been superfluous, led to a revision of the views regarding the needs of the secondary resection Bowen and Day report the postmortem findings in a case of regional ileitis nine years after symptomatic recovery following ileo colostomy The ileum, previously affected, was at the autopsy shown to be fibrosed and sclerotic the lumen almost obliterated by stenosis and by multiple adhesions Complete healing of the ileum had been affected by the short circuiting procedure

In 1939, Ginzburg, Colp and Sussman published 14 cases of short circuiting operations for ileitis, transection of the ileum being regularly carried out Again they were convinced of the lack of necessity for any subsequent resection, the initial lesion drying up and undergoing atrophy after the short circuiting, fistulae disappearing, abdominal masses resolving The x ray studies of Sussman convincingly demonstrated no trapping in the excluded loop and good intestinal function through the new stoma

In 1941, Colp and Ginzburg published a report of ileo-colostomy with exclusion as practiced in 22 cases of terminal

ileitis with no deaths, 3 of the series showed recurrent symptoms. Four of the cases were re explored because of persistent diarrhea, in all 4, healing of the original site of infection in the terminal ileum was clearly demonstrable and no further resection was attempted. Six cases had abdominal wall fecal fistulas before operation, after the short circuiting procedure, five of the fistulas healed and ceased to discharge content. In 1942 Ginzburg and Garlock published 54 cases of ileo colostomy with exclusion with no operative mortality, with two recurrences of the disease in the proximal ileum and with 5 cases with persistent clinical symptoms. Contrasted with this were 23 cases of primary resections with four deaths and three recurrences.

In 1945, the largest group of cases from the Mount Sinai Hospital was published (Garlock and Crohn), covering a twelve year experience with the surgical treatment of chronic regional ileitis. The series comprised 164 cases of enteritis, terminal ileitis and combined ileo colitis, most of which had been operated upon by various surgeons in that institution (137 cases); the remaining 27 cases had been operated elsewhere but reported for observation because of persisting symptoms. The inclusion of these latter cases, which represent failures of previous procedures, depresses the statistical value of the total end results of the series but had been included nevertheless in the interests of scientific accuracy. The results may be seen in table 10.

TABLE 10.—Surgical Treatment of Chronic Regional Ileitis

	Number	Deaths		Recurrences	
Ileo colostomy with exclusion	65	0		9	(13.8%)
One stage resection	55	9	(16.3%)	9	(19.5%)
Two stage resection	5	3	([illegible])	8	(36.3%)
Combined ileo colitis	19		(10.5%)	3	(1[illegible]6%)

By a process of comparison the advantages of the ileo colostomy with exclusion are obvious. The mortality rate was nil, the recurrence rate (as of that date) was moderate but yet considerable. The group of cases comprising primary resection was less satisfactory, a considerable mor

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failed to result in amelioration of symptoms or relief in 36 3 per cent of this smaller series These are the distressing and depressing cases that create skepticism as to the success of any or all surgical procedures as adapted to the cure of regional ileitis

4 The Lahey Clinic favors a Mikulicz type of resection for ileitis, the diseased ileum and the ascending colon are brought out on the surface of the abdomen, exteriorized and resected extraperitoneally A secondary closure of the enterostomies is later performed Marshall in 1940 and again later in 1943 reported a ten year survey of 55 patients surgically treated The operative mortality was 5 5 per cent, in a follow up that covered 42 patients of the series there were five recurrences or 9 6 per cent In the presence of abscess or infection a short circuiting procedure is preferred as a first stage with a later secondary resection Note again that even here the secondary resection is regarded as essential

Of this series, 35 cases underwent the Mikulicz procedure with but one death, a highly commendable record

5 The group at the Mayo Clinic seem to prefer a two stage operation In 1937 Pemberton and Brown reported 39 cases of ileitis treated by two stage short circuiting and resection with three deaths They allowed three weeks to six months between the first and the second procedure Transection of the ileum as part of the first operation was always mandatory In 1938, Dixon reported 40 operated cases the procedures were evenly divided between primary resection two stage operations and short circuitings alone Again the gross mortality was low, 10 per cent

In 1939 Clark and Dixon questioned the utility of the short circuiting operation per se they considered 50 per cent at best the estimate of cure after such a procedure, and emphasized the high percentage of postoperative recurrences following short circuiting procedures as the sole type of operation

tality was apparent, nor did there appear to be any compensation for the greater risk since the recurrence rate of resection was even greater than that of the exclusion operation Here the longer follow up period of the earlier resected cases may well be a factor since recurrences were noted once eight years and once twelve years after the original operation, the intervening years having been a period of apparent perfect health Bockus had already noted a recurrence of postoperative ileitis nine years after apparent good health

It cannot be too strenuously emphasized that transection of the ileum proximal to the diseased area is a sine qua non to the success of any operation (Lewisohn) In this present group of 222 cases of regional ileitis, 8 cases had been operated elsewhere, without transection of the ileum All of them were in distress because of persistent symptoms In one case the mere transection of the ileum at a subsequent operation resulted in control of the diarrhea and a gain of 50 pounds of weight In many of the others, radical excision of the lesion was necessitated by the omission of the former surgeon properly to exclude the primary focus of disease The remarkable case published by Forbes and Duncan in which a true ileo vesical fistula was cured only after transection of the ileum had been secondarily accomplished is most instructive

To return to the analysis of end results of 164 surgically treated cases as published by Garlock and Crohn The two stage operation consisting of a primary ileo colostomy with transection of the ileum, followed some time later by a resection of the primary focus of disease, constituted the most distressing group Naturally so, because these cases all represent failures of short circuiting procedures the second stage of the operation was forced by the gravity of the persisting symptoms at the original site of disease Actually, they represent failures of the first stage short circuiting procedure The forced secondary operation was fraught with a moderate mortality (12 0 per cent) but

of resection was employed in two of his cases, probably the first time this modified form of resection had been mentioned in the literature Cutler (1939) even went a step further and suggested that surgery was not a cure for ileitis, recurrences following radical surgery were frequent, patients may recover spontaneously He suggested the retention of the case in the hands of the family physician as possibly a good solution

In 1942, Warren and Miller reported 26 resections for ileitis with only one death, however, in the follow up, only 6 patients were free of disease, most of them incapacitated

These reports published from Boston represent individual opinions None of the series of cases was large the opinions expressed seem to be depressing though contrary to the more optimistic conclusions of those with far greater numbers of cases and with equally critical scientific analyses of their results The recent critical editorial (Starr), "Is There an Adequate Therapy for Regional Enteritis? concedes that surgery offers the best opportunity for palliation and the control of regional enteritis, but emphasizes that the end results leave much to be desired

The most disappointing effects are seen when attempts have been made to perform resections of the ileum in continuity with end to end anastomosis of the small bowel Procedures such as this one are insufficient unphysiologic and lead to skepticism (3 such cases in this present group) This same criticism does not apply to high jejunal involvement where local resection is eminently successful

8 Recurrences There is the growing realization of the increasing incidence of recurrences following all types of surgical interference increasing incidence because the longer the follow up the greater the possibility for late recurrences, since by now it is recognized that recurrences can and do occur eight, nine or even twelve years after the operative procedure

Recurrences are mentioned in the literature almost as soon as operative procedures had been initiated (Homans and

In 1941, Mayo and Judd reported a full 100 cases, 64 of which underwent the two stage operation, with a 3 per cent mortality, the average length of time between the two stages was 14 4 months With multiple procedures in the complicated cases, Brown and Donald had a higher mortality of 9 per cent for a larger series (178 cases) They suggest surgical removal of the diseased segment of bowel "a two stage procedure is better than a one stage operation"

Thus, the Mayo group still prefer the two stage procedure, eschewing the single stage resection and not accepting a simple short circuiting operation as sufficient

6 Bockus clings to his preference for single stage resections He draws support from the report of Rhoads who collected from the literature 125 cases in 51 of which a side tracking procedure alone had been carried out with a high percentage of recurrence (47 per cent) Bockus feels that considerable progress in the course of the disease may take place between the two stages of a double procedure, a point which is flatly contradicted by the experience of other writers He believed in 1940 that a one stage operation could be safely performed Again in 1944 he feels that the chances of cure are 2 to 3 times greater with primary resection than with short circuiting procedures His medical cases were submitted to resection with a mortality of 7 7 per cent and only one late recurrence out of 18 cases He retains throughout his confidence in primary resection, his series of cases is, however, small

7 Pessimism as regards results in the operative treatment of ileitis seems to spring from some, but not all, of the Boston surgeons Already in 1935 Mixter in a questionnaire to various surgeons reported a 20 per cent recurrence rate after operative procedures In a small series of 11 difficult cases with complicated and multiple procedures, his mortality rate was 36 per cent Mixter restricted his surgical procedures to, and advocated the use of resection in one or two stages The Mikulicz technic

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Recurrences are mentioned in the literature almost as soon as operative procedures had been initiated (Homans and

Hass, Shearer and Jackson, Oppenheimer, Felger and Schenk, Koster et al [15 per cent of recurrences]) These recurrences occur almost uniformly in the ileum just proximal to the new anastomosis, 6 to 8 inches in extent, the pathology of the recurrence grossly and histologically resembling the initial lesion Skip areas above the local recurrence are unusual, though exceptionally these recurrences may extend continuously or in an interrupted fashion throughout the remaining ileum and the jejunum Internal fistulous tracts may originate at the anastomosis, more rarely from the involved segment of recurrent ileitis

It is difficult to explain the rationale and method of propagation of such recurrences, particularly when the operation had been performed by a competent surgeon, one of experience in recognizing the highest possible skip lesion In the best of hands, where the transection isolating the ileal lesion has been placed high and far distant above any suspiciously involved areas, approximately 15 to 20 per cent of recurrences are conceded

Two possible methods of propagation of the recurrences suggest themselves

(a) The surgeon is unable to recognize the uppermost skip lesion and makes his anastomosis too low in the ileum That this mistake is due to ignorance or inadvertence or inexperience is gainsaid by the fact that recurrences occur at the hands of the most careful, meticulous and experienced surgeons Obviously, if it be a mistake in judgment, it occurs because the mucosal or submucosal infiltration is so minimal as to preclude recognition by palpation or inspection of the wall of the small gut which is utilized for the anastomosis It seems likely that such skip areas may and do escape the vigilance of even the most adept surgeons If this be the explanation then the loop of ileum chosen for the anastomosis must be high and far away from any suspected pathologic involvement Such a high choice invites the danger of nutritional disturbances by sacrificing too much mucosa necessary for food absorption and by inviting the possibility of diarrhea

(b) The recurrences are due to the persistence of a nidus of residual infection, outside the intestinal wall, most likely in the retained and inflamed mesenteric lymph nodes. If such were the case, then recurrences should occur with greater frequency after short circuiting operations than after radical resections, a fact which is contradicted by the table of figures. In the radical excisions of the lesion, it is usual to remove the succulent enlarged lymph nodes with the mesentery and with the original lesion, a deep angular resection of the mesentery being performed by most experienced surgeons. However, even with such a radical excision the recurrence rate (19.5 per cent) is higher than with short circuiting procedures (13.8 per cent) (Garlock and Crohn). If the lymph nodes actually constitute the source of residual infection and reinfection, it is necessary to postulate the spread against the normal lymphatic flow which is from the intestine to the lymph nodes rather than the reverse. This is contrary to physiologic knowledge though retrograde reinfection and retrograde metastases do occur as in carcinoma. Further it has been shown on secondary explorations after short circuiting procedures that when re examined the originally inflamed lymph nodes are now diminished in size and show retrogression of the infection.

In this present series of 222 cases of ileitis the types of operation which had been carried out are given in table 11.

TABLE 11.—*Types of Operations for Ileitis*

	(Present Series)
Primary resection	30 cases
Ileo transverse colostomy with transection of ileum	5 cases
Ileo transverse colostomy without transection of ileum	1 case
Mikulicz procedure	1 case
Ileo sigmoidostomy with transection of ileum	[illegible] cases
Resection of ileum in continuity	1 case
Ileo transverse colostomy with transection followed by second stage resection of lesion	10 cases
Total	108 cases

The rate of recurrence for this group will not be quoted because so many of these cases were operated elsewhere

and came under observation because of secondary aggravation of symptoms To a large extent they include a "trouble" group, specially referred because of postoperative distress symptoms To attempt to draw conclusions as to the incidence of or percentage of recurrence from such a group of unfortunates would only enhance pessimism regarding surgery in ileitis and would not be a true overall critical analysis of the problem A better idea of mortality and recurrence rate is obtained by referring back to the figures (table 12) quoted by Garlock and Crohn in their review of 137 cases personally chosen and supervised and operated at the Mount Sinai Hospital, New York City

TABLE 12 —*Operation and Recurrence in Ileitis (Garlock and Crohn)*

	Cases	Deaths	Recurrences
Ileo colostomy with transection	5	0	6 (10 5%)
One stage resection	45	6 (13 3%)	6 (15 4%)
Two stage resection	16	2 (12 5%)	4 (28 6%)

Diagnosis and Treatment of Recurrences

After operation, the patient usually regains strength and weight and appetite hemoglobin values improve, diarrhea is relieved, fever ceases True, the diarrhea after short circuiting procedures may persist to a distressing degree for a few weeks, even months, but almost invariably when weight and strength return the number of defecations is diminished to a normal of two to three daily movements without pain or urgency

A recurrence of the disease is marked by the return of fever, by loss of weight increasing anemia and increasing diarrhea The radiographic demonstration of irregularity of the mucosal pattern of the "new" terminal ileum, narrowing of the lumen, rigidity and distortion in the 6 to 8 inches of small bowel just proximal to the new anastomosis confirm the existence of a recurrence (fig 41) These recurrences of disease are usually localized in the area just proximal to the anastomosis rarely do they extend upward by skip lesions to involve the upper small intestine, and very rarely do they involve the colon, sigmoid or rectum The recurrence is best demonstrated by barium

enema, the possible involvement of a higher segment of small bowel must be established or excluded by the barium meal study of higher ileum and jejunum. Many of these recurrences are exceedingly mild, fever is absent, loss of weight minimal, diarrhea and anemia being the only presenting symptoms. Even the diarrhea is undependable as a sign of recurrence since postoperative diarrhea even in successfully operated cases is not unusual. One depends

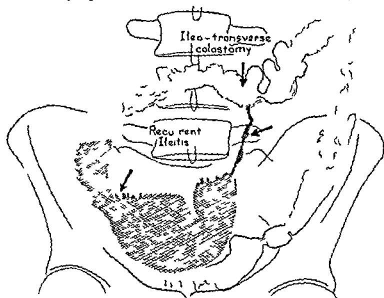


Fig. 41.—Recurrent Ileitis Proximal to a Distal Ileo-Transverse Colostomy. Stringy sign new terminal ileum; proximal dilation of small bowel. Conservative medical therapy; patient under observation eight years. Good general condition.

therefore to a large extent upon the radiographic interpretation of the loop proximal to the anastomosis; such interpretation is not infallible, just as the original radiographic diagnosis of a lesion in the terminal ileum is not always accurate; errors of omission and of commission are likely to occur (figs. 42 and 43).

Recurrences are likely to be noted soon after operation; in fact, most of them occur within the first year of convalescence as noted in this present series (table 13).

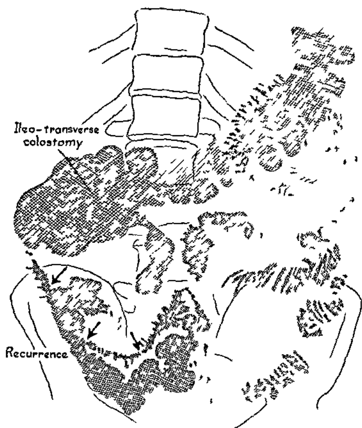


Fig 42—Extensive Recurrent Ileitis Proximal to Ileo Transverse Colostomy *Note the involvement of several loops of the "terminal ileum*

TABLE 13—*Recurrences in Present Series after Operation*

Immediate recurrences	6 cases
Within 6 months	4 cases
Within 1 year	4 cases
Within 2 years	1 case
Within 3 years	3 cases
Within 4 years	2 cases
Within 5 years	3 cases
Within 6 years	[illegible] cases
Within [illegible] years	1 case
Within 1[illegible] years	1 case
Within 16 years	1 ca[illegible]
Total	[illegible]8 cases

It is not to be implied from this table that recurrences are limited in time, postoperatively In fact there is probably no time limit of follow up which precludes the possi



Fig 43—Recurrent Ileitis Proximal to Ileo Colostomy Recurrence six weeks after operation

bility of a recurrence Bockus refers in detail to a case in which, presumably nine years previously, a resection of the terminal 10 inches of the ileum had been performed for a lesion undoubtedly regional ileitis in nature The patient was well for nine years, suffered recurrent symptoms and was re explored surgically A recurrent ileitis involving the area of ileum proximal to the ileo transverse colon anastomosis was demonstrated My own experience has furnished two instances of very late recurrences

Case 1 I *S* (Serial No 170) Male age [illegible] years Nine years previously he underwent a resection of the terminal ileum and ascending colon

for a regional ileitis involving the last eight inches of the small bowel The patient remained well and free of symptoms for approximately nine years or until six months ago when he developed a spontaneous fecal fistula breaking through the anterior abdominal wall at the site of the scar of the previous surgical incision Exploratory laparotomy now demonstrated a recurrent ileitis involving the proximal ten inches of the 'new' terminal ileum A two stage ileo sigmoidostomy followed by a resection of the involved recurrent segment of ileum and its connected transverse colon resulted in restitution of health

Case 2, F R K (Serial No 83) Male age 34 years In a second case one which constituted one of the earliest cases of ileitis seen and diagnosed the terminal ileum had been resected for regional ileitis in 1930 The uneventful recovery was followed by twelve years of perfect health and efficiency Abrupt recurrent symptoms resembling intestinal obstruction required an emergency operation At the exploration an obstruction at the site of the anastomosis and due to a severe acute recurrent ileitis was demonstrated An attempt to resect the lesion in the face of the obstruction resulted in a fatal termination

Recurrences with gross intestinal hemorrhage are rare, with abdominal wall fistulation somewhat more frequent Recurrences in the colon, in the rectum and in the upper small intestine have been noted, fortunately infrequently, but represent a sad picture since little of a further surgical nature can be attempted Sometimes permanent ileostomy above the recurrent lesion is the only means of saving life

The very rare involvement of the colon in recurrent ileitis is a very interesting negative phenomenon For though there is no equivalent of an ileo cecal valve of Bauhin at the new anastomosis and though the recurrent ileitis empties unguardedly into the exposed colon, the natural immunity of the colonic mucosa to the ileal infection seems to preserve it from involvement by extension This was impressively demonstrated in one particular case an ileitis had been resected 18 years previously, the nature of the lesion being little suspected Recurrence of symptoms occurred, at the subsequent operation eighteen years later the recurrent lesion and attached ascending colon were resected en masse the colon was free of disease though probably for most of the long period the recurrent ileitis emptied its content into the large bowel at the anastomosis

The Treatment of Recurrent Ileitis

Fortunately most of the recurrences are mild. Many of them can be controlled by conservative medical treatment. Such therapy consists of drugs that control the frequency of the diarrhea, particularly opiates; combating the anemia by intramuscular injection of crude liver extract and vitamin B complex; the administration of amino acid preparations or protein hydrolysates by mouth in large amounts, 6–8 ounces per day; rest, warm climate and sunshine. The insoluble sulfa derivatives, sulfasuxidine and sulfathaladine are usually administered though their value is often questionable; occasionally a brilliant therapeutic result is achieved. An increasing number of cases of recurrent ileitis seem to do well and retain only mild clinical symptoms under conservative medical therapy. So much so that surgical intervention should be reserved only for those cases which refuse to improve under general therapeutic measures or which develop complications such as fever and abdominal wall or perirectal fistulas. A remarkable instance of spontaneous cure of recurrent ileitis and jejunitis is seen in the case reported by Pessagno. A boy, aged 13, underwent an obstructive resection of terminal ileum and cecum for regional ileitis. A recurrence of the symptoms plus external fistulas forced a secondary resection. A persistent or recurrent fistula now complicated by obstruction necessitated a third operation. At the second operation an all extensive involvement of the terminal ileum and the jejunum were noted. In spite of the extensive evidences of recurrences throughout the small bowel and the almost hopeless prognosis, the patient when last seen was in excellent condition and making a rapid recovery: appetite good, one or two stools a day, wounds entirely healed. Unfortunately the period of follow up was limited to less than a year.

A similar spontaneous regression of a recurrent ileitis may be observed in an interesting case in this present series

Case D G (Serial No 63) Male age 37 years Nine months ago operated for a supposed acute appendicitis At exploratory operation an acute ileitis was observed Six months ago re operated because of recurrent symptoms ileo transverse colostomy performed for terminal ileitis At the time of operation two ileo ileal internal fistulas were demonstrated and another fistula from ileum to sigmoid was demonstrated Six months later radiographic studies showed an extensive recurrence in the loop of ileum proximal to the new anastomosis One year later the patient reported being in good health and free of symptoms X ray examination at this time showed spontaneous regression of the recurrent ileitis and no evidence of the ileo sigmoid fistula Two years later the follow up of this interesting case reported perfect health except for slight diarrhea

Surgical intervention in recurrent ileitis becomes necessary when fistulas appear, when the recurrence shows signs of extension, when the general nutrition is compromised and the anemia becomes progressive Continued fever is further an indication for surgery

The surgical procedures for the cure of recurrent ileitis consist of *a further short circuiting procedure*, usually an ileo transverse colostomy distal to the previous anastomosis again with transection of the intervening ileum so as to exclude the newly involved segment Some surgeons also transect the transverse colon distal to the first anastomosis, bringing the proximal cut end out on the abdominal wall as a temporary or mucous colostomy A second stage procedure is now required to excise the recurrent ileitis and the attached transverse colon Other surgeons, following the principle of short circuiting, merely make the new anastomosis, transect the ileum so as to exclude the involved segment and make no attempt further to resect the recurrent lesion It is too soon to say which is the preferable surgical approach It is certainly true that one operation is always better than a two stage procedure, providing it suffices to heal the recurrence The mortality of such operation for recurrent ileitis is exceedingly small, and the improvement in well being weight and strength is very satisfactory Unfortunately, too many instances can be cited of extensive and rapidly extending recurrences that defy surgical inter

vention Two such cases in this series will demonstrate the almost malignant nature of the rapid and universal involvement of the small bowel by recurrent ileitis

Case I M (Serial No 229) Male, 17 years of age *Six months* of abdominal pain and diarrhea Regional ileitis involving the terminal 18–24 inches *of the terminal* ileum was demonstrated radiographically and at the exploratory operation ileo transverse colostomy with exclusion of the ileum Recurrent symptoms *occurred* exactly *one* year later with rapidly down hill course At exploratory laparotomy thirteen months after the original short *circuiting* procedure, a diffuse ileo jejunitis extending up to the duodenum was demonstrated No further surgical procedure was attempted

Case A M (Serial No 110) Female single 29 years of age Eight years of *alternating* diarrhea *and* constipation loss of 50 pounds of weight Eleven months ago resection of terminal *2 feet* of ileum (and ascending *colon*) for terminal or regional ileitis Six months later because of rapid recurrence of symptoms the patient again underwent surgical exploration The entire ileum proximal to *the* anastomosis and the jejunum were the seat of extensive recurrent inflammatory disease *Persistent* abdominal wall fecal fistulas *resulted after* the last *and* futile exploration The prognosis is absolutely hopeless

Secondary recurrences *do* occur, *fortunately* infrequently These are usually met when the indications for surgery become mandatory by a third anastomosis, usually an ileo sigmoidostomy, *again* with transection of *the* ileum above *the* secondary recurrence These *cases, too,* though infrequent, occasionally do well, the diarrhea following such repeated surgery is not excessive

The most recent suggestion regarding treatment for extensive diffuse ileitis or ileo jejunitis *comes from* a West ern group *Vagotomy* has been experimentally tried for the relief of symptoms and possibly the cure of severe ulcerative colitis The idea has been *extended* to cover also the possible very serious forms of ileo jejunitis Considering that a vagotomy is followed by *atony* when applied to the stomach it may well be that the *putting at* rest of the small intestine by the same surgical procedure can be similarly accomplished Certainly the idea is worth consideration *

Dennis C Eddy F D *Frykman* H N McCarthy A N and Westner D Ann Surg *1 8* 479 *1948*

Case D G (Serial No 53) Male age 37 years Nine months ago operated for a supposed acute appendicitis At exploratory operation *an acute ileitis* was observed Six months ago re operated because of recurrent symptoms ileo transverse colostomy performed for terminal ileitis At the time of operation two ileo ileal internal fistulas were demonstrated and another fistula from ileum to sigmoid was demonstrated Six months later radiographic studies showed an extensive recurrence in the loop of ileum proximal to the new anastomosis One year later, the patient reported being in good health and free of symptoms X ray examination at this time showed spontaneous regression of the recurrent ileitis and no evidence of the ileo sigmoid fistula Two years later the follow up of this interesting case reported perfect health except for slight diarrhea

Surgical intervention in recurrent ileitis becomes necessary when fistulas appear, when the recurrence shows signs of extension, when the general nutrition is compromised and the anemia becomes progressive Continued fever is further an indication for surgery

The surgical procedures for the cure of recurrent ileitis consist of a further short circuiting procedure, usually an ileo transverse colostomy distal to the previous anastomosis again with transection of the intervening *ileum* so as to exclude the newly involved segment Some surgeons also transect the transverse colon distal to the first anastomosis, bringing the proximal cut end out on the abdominal wall as a temporary or mucous colostomy A second stage procedure is now required to excise the recurrent ileitis and the attached transverse colon Other surgeons, following the principle of short circuiting, merely make the new anastomosis, transect the ileum so as to exclude the involved segment and make no attempt further to resect the recurrent lesion It is too soon to say which is the preferable surgical approach It is certainly true that one operation is always better than a two stage procedure, providing it suffices to heal the recurrence The mortality of such operation for recurrent ileitis is exceedingly small, and the improvement in well being weight and strength is very satisfactory Unfortunately, too many instances can be cited of extensive and rapidly extending recurrences that defy surgical inter

vention Two such cases in this series will demonstrate the almost malignant nature of the rapid and universal involvement of the small bowel by recurrent ileitis

Case I M (Serial No 279) Male 17 years of age Six months of abdominal pain and diarrhea Regional ileitis involving the terminal 18-24 inches of the terminal ileum was demonstrated radiographically and at the exploratory operation ileo transverse colostomy with exclusion of the ileum Recurrent symptoms occurred exactly one year later with rapidly down hill course At exploratory laparotomy thirteen months after the original short circuiting procedure a diffuse ileo jejunitis extending up to the duodenum was demonstrated No further surgical procedure was attempted

Case A M (Serial No 110) Female single, 29 years of age Eight years of alternating diarrhea and constipation loss of 50 pounds of weight Eleven months ago resection of terminal 2 feet of ileum (and ascending colon) for terminal or regional ileitis Six months later because of rapid recurrence of symptoms the patient again underwent surgical exploration The entire ileum proximal to the anastomosis and the jejunum were the seat of extensive recurrent inflammatory disease Persistent abdominal wall fecal fistulas resulted after the last and futile exploration The prognosis is absolutely hopeles

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* Dennis C Eldy F D Frykman H N McCarthy A N and Westne D Ann S g 1 8 479 1948

12 Acute Regional Ileitis

IN THE ORIGINAL description published in 1932, cases of acute regional ileitis were recognized and described The clinical picture was similar to that of acute appendicitis, namely, generalized abdominal colic, pain, tenderness over the right lower quadrant, fever up to 101 or 102 F The white blood count was elevated A mass without active abscess formation was fairly constant At operation, the findings were those of a mass of adherent and inflamed loops of ileum, the terminal coil being red, edematous, soggy and brilliantly congested, the mesentery of the gut was thickened and edematous and contained enlarged inflamed mesenteric lymph nodes Clear or cloudy fluid in small *amount was present in the peritoneal cavity In rare cases*, an abscess cavity containing thick aqueous but not foul smelling pus was encountered A general statement was made that some cases resolved without operative interference, others passed transitionally into the chronic phase of the disease It was presumed that the acute was but one phase of the chronic disease The number of cases was too small and the follow up too recent to allow of any scientific statements other than to describe the clinical and pathologic picture *Jackman shortly thereafter reported 2 almost* identical cases in which the acute picture of ileitis represented only a flare up of the process upon the basis of an old chronic inflammatory lesion in the terminal ileum Both cases were successfully resected Erb and Farmer reported 4 cases of acute ileo colitis in children Meyer and Rosi described 8 cases of regional ileitis, 4 of which were of the

acute type, 3 of these 4 *acute* cases underwent spontaneous resolution. Rocker described a case of thickening of the terminal ileum, apparently an acute regional ileitis, in a child aged 5 years.

The ample literature that followed from the publications of many surgeons, Clute, Ladd, Harris, Bell and Brunn and our own *present* group in this series amply bore out the facts as set down in the earlier publication. Sufficient time and experience and follow up has, however, elapsed to warrant a more complete clinical picture, to elaborate upon the life cycle and prognosis of such cases. The surgical attack upon acute ileitis has passed through several phases and may now be recapitulated in its present and probably its final formulation.

The group in *this* present series comprised 16 cases, none of them more recent than one year, all of them observed a sufficient time to allow for the creation of a life history of this, the acute phase of ileitis.

The sex distribution is about equal; the ages vary from 2½ to 37 years, an average of 23½ years at onset, in contrast to 27½ years for the chronic phase of the disease. The difference *in* age incidence probably represents the gap between acute onset and the final development of the chronic picture. Many cases *of* acute ileitis occur in young children. Thus *the* well described case *of* Erb and Farmer in a 2½ year old child with complete autopsy findings, that of Harris in a 5 year old female child, Schiff 1¼ years of age. Warren and Sommers *observed* that the acute form of ileitis is more severe in young children, since the diameter of the bowel is smaller and *edema* easily produces obstruction.

Three of 8 cases reported by *Meade* occurred in children 6, 8 and 9 years of age respectively. Megret's case involved a child 3 years of age with successful resection of the involved ileum at the time of exploration.

The pathologic involvement as seen at operation showed

the terminal ileum as the constant seat of involvement (table 14)

TABLE 14—*Extent of Pathologic Involvement*

	(Present Series)
4 inches of terminal ileum	2 cases
5 inches of terminal ileum	2 cases
6 inches of terminal ileum	1 case
8 inches of terminal ileum	2 cases
15 inches of terminal ileum	1 case
18 inches of terminal ileum	2 cases

Skip lesions as seen in chronic ileitis are not mentioned by the operating surgeons, an important observation, since it is a clear indication of the fact that the primary seat of the disease is regularly at the terminal ileum, the skip lesions representing a secondary and later extension in time and in site The lesion at operation is characteristic, the terminal loop of ileum being bright red, edematous, soggy, congested, the mesentery thickened, the lymph nodes enlarged in some cases, not remarked in others In one case, an abscess cavity was observed, surrounding a perforation of the terminal loop of ileum, the abscess containing fresh pus The serosa of the ileum is covered by a serofibrinous exudate free fluid being seen in the peritoneal cavity The pathologic or histologic findings in acute ileitis are almost identical with those of chronic ileitis A greater degree of edema is present, leukocytic invasion is more prominent The villi show loss of epithelium and become mere shadows Very little slough of tissue is to be noted The serosa is edematous, the blood vessels tremendously engorged The lymph nodes are extremely edematous with marked hyperplasia of the germinal centers (Harris)

The clinical manifestations of acute ileitis show but little variation The onset of symptoms varies from one to three days in most cases, extending up to five weeks The acute, often fulminating onset is characterized by pain in the general abdomen or in the right lower quadrant, the pain, colicky in nature present in all cases, accompanied

by fever, ranging from 100 to 103 F, the curve being constantly elevated and not remitting. Nausea and vomiting are not outstanding symptoms, each of them mentioned only in 2 cases, an important point in differentiation from acute appendicitis. A mass in the right lower quadrant of the abdomen was clearly palpable in 3 of the cases.

Diarrhea occurred in 11 of the 16 cases; constipation is clearly mentioned once only. The diarrhea may be and is often transient; may last one day, and be followed by normal stools and constipation, or may last throughout the acute phase of the disease.

Hematemesis and tarry stools occurred in one case; transient intestinal obstruction once. Other unusual manifestations are purpura hemorrhagica (once), erythema nodosum (once), arthralgias (once); these latter unusual signs and symptoms, though rare in the acute phase, link this abrupt onset with that of the more fully developed clinical picture of chronic ileitis.

The radiographic picture, an examination which is usually undertaken some days or weeks after the exploratory laparotomy, may demonstrate positively the involvement of the terminal ileum. In 8 of the 16 cases which were subjected to roentgen study the localization and the extent of the lesion could be clearly noted. The "string sign," so characteristic of the fully developed chronic phase of the disease, is missing because the cicatrization and the contraction of the lumen of the ileum has not yet had time to develop. The mucosal pattern of the terminal loop of ileum is disturbed, the lumen narrowed, the proximal gut dilated, the contour irregular and shaggy. The extent of involvement as noted by the radiologic survey corresponds almost identically with that seen at operation (figs. 44 and 45).

The diagnosis concerns itself practically with the differentiation of acute ileitis from acute appendicitis. The one and only possible clue lies in the presence of or absence of diarrhea, since as a rule ileitis is accompanied

by diarrhea (11 of 16 cases) and appendicitis by constipation Unfortunately, both symptom complexes afford exceptions to the rule Ileitis may be accompanied by constipation, though *rarely (once in this series only)*, *acute* appendicitis may occur with and in the presence of diarrhea To all intents and purposes, however, appendicitis is asso



Fig 44 — Acute Terminal Ileitis Involving only Two Inches of the most Distal Ileum Proximal to the Ileo Cecal Valve Confirmed by operation

ciated with constipation and vomiting diarrhea has been *noted though exceptionally* Endemics of acute gastro enteritis with severe diarrhea may be complicated by a rare incidence of acute suppurative appendicitis (Crohn [60])

Acute mesenteric lymphadenitis simulates both acute ileitis or acute appendicitis and cannot by any *clinical* symptoms be identified Whether acute mesenteric lympha

denitis and acute ileitis are phases of the same disease process if not identical, has been suggested and is still an open question (Jackson) Involvement of the terminal ileum in acute mesenteric lymphadenitis has been mentioned (Strombeck), but the transition of acute lymphadenitis to chronic regional ileitis has not been observed



Fig 45 — Acute Ileitis Spontaneous Healing One of two brothers The other brother with subacute onset developed the clinical picture of chronic granulomatous ileitis

The prognosis in acute ileitis is good only one case with fatal termination was observed following an ill advised attempt at resection during the acute severe toxic febrile state of the disease Four cases were not subjected to any operation 2 of these cases are well to date (4 and 5 years of follow up) one has passed into the chronic granulomatous stage one has been lost to follow up

The remaining 11 cases were explored appendectomy performed in eight instances with three subsequent and

by diarrhea (11 of 16 cases) and appendicitis by constipation. Unfortunately, both symptom complexes afford exceptions to the rule. Ileitis may be accompanied by constipation, though rarely (once in this series only), acute appendicitis may occur with and in the presence of diarrhea. To all intents and purposes, however, appendicitis is asso-



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Acute mesenteric lymphadenitis simulates both acute ileitis or acute appendicitis and cannot by any clinical symptoms be identified. Whether acute mesenteric lympha-

TABLE 16.—*Catalogue of Cases of Acute Ileitis from the Literature*

		No. of Cases	Subsidence	Died	Resected	Enterostomy
1934	Jackman	2			1	
1935	Erb and Farmer	4	2	[illegible]		
1936	Probstein and Gruenfeld	3	2			2
	Meyer and Pom	5	3		2	
	Koster et al	6	6			
19[illegible]	Brown T W	6	3			
	Mailer	2	1			
	Pugard and Henke	1	1			
1938	Kross I	1	1			
1939	Lehman		[illegible]			
1940	Harris	1			1	
	Eliason and Johnson	1		[illegible]		
1943	Smithy	[illegible]	4		1	
194[illegible]	Ebrill	1				
		[illegible]	[illegible]	[illegible]	[illegible]	—

Three questions arise (a) Is acute ileitis a distinct entity or is it a part of the picture of chronic regional ileitis? (b) What is the consensus as to the eventual outcome of cases of acute ileitis? (c) What is the proper surgical or medical treatment of acute ileitis?

(a) *Distinct Entity or Part of Chronic Regional Ileitis?*

Acute ileitis is undoubtedly an individual phase of regional ileitis It occurs most frequently as an initial phenomenon capable of complete subsidence in from 25 per cent to approximately 50 per cent of the cases, in the remainder advancing to the classic picture of chronic granulomatous ileitis On the other hand in furtherance of the concept of identity of acute and chronic ileitis acute ileitis may often be regarded as an abrupt exacerbation of the chronic phase of the disease In many cases a previous history of diarrhea and abdominal pain can be elicited if carefully sought after an occasional bout of temperature, a previous rectal operation Out of this low grade generally unrecognized and unacknowledged course will occur an acute severe episode this exacerbation will again subside and the future course will be identical again with that

consequent abdominal wall fistulas (two of which closed spontaneously) Following the exploratory operation 2 of these cases became well and free of symptoms and of radiographic evidence of disease, the other 9 passed into the granulomatous phase of the disease Of these 9 cases which passed into the chronic inflammatory stage 4 are still not operated upon, 4 have undergone a short circuiting surgical procedure (ileo transverse colostomy) and are well, one was subsequently resected and is well The aftermath of these cases may be summarized as in table 15

TABLE 15—*Follow up of Acute Ileitis*

	Cases
Unoperated—4 cases	
Spontaneous resolution	2
Chronic granulomatous phase	1
No follow up	1
Operated—12 cases	
Resection—death	1
Spontaneous resolution—well	2
Chronic granulomatous phase	4
Subsequent short circuiting operation	4
Subsequent resection	1
Total	16

It will be noted that the operative procedures, apart from the initial surgical exploration, were all carried out months or several years subsequent to the acute phase of the disease Most of the cases during the acute onset were subjected to appendectomy only In only the one instance where death occurred was resection attempted during the initial grave onset of the acute ileitis, this death occurred elsewhere in spite of the caution and warning of the gravity of such a bold attack

The literature on acute ileitis is replete with good illustrative cases, most of which have been carefully observed and reported with prolonged follow up At least 50 to 60 cases have been adequately catalogued, the clinical picture following in most instances the pattern as originally described and as amplified and confirmed by subsequent authors (table 16)

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1936	Probstein and Gruenfeld	3	2			2
	Meyer and Rosi	5	3		2	
	Koster et al	6	6			
193[illegible]	Brown P W	6	3			
	Mailer	[illegible]	1			
	Bisgard and Henske	1	1			
1938	Kroes I	1	1			
1939	Lehman	[illegible]	5			
1940	Harris	1			1	
	Eliason and Johnson	1	5	3		
194[illegible]	Smythy	5	4		1	
194[illegible]	Ebrill	1				
		—	—	—	—	—
		39	33	5	5	

Three questions arise (a) Is acute ileitis a distinct entity or is it a part of the picture of chronic regional ileitis? (b) What is the consensus as to the eventual outcome of cases of acute ileitis? (c) What is the proper surgical or medical treatment of acute ileitis?

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of chronic regional ileitis (Brown, Lehman, Eliason and Johnson, Smithy) Lyall even expresses the view that chronic regional ileitis represents only the end stages of acute ileitis with subsequent fibrosis and cicatrization "The *process is primarily an acute one which tends to* subside so that the appearance thought by some to indicate a chronic inflammation are really attempts at repair"

(b) *The Eventual Outcome of Cases of Acute Ileitis*

In my own series, only 25 per cent (4 cases) showed *complete resolution as judged by subsidence of all symp*toms, by the change of a positive x ray picture to that of a normal roentgenogram The follow up, covering a sufficient number of years (10 to 14 years in some instances), allows of the presumption that these patients will continue well, even though we now know that recurrences of ileitis (after even supposedly curative operations) may occur after an equally long period of observation In all of them, x ray studies were made soon after convalescence and the change from a positive to a negative x ray examination was noted The time required for healing or for a negative roentgenogram varied from 1 month to as long as 14 months in the most protracted case The gradual disappearance of the lesion could be ascertained by comparing successive x ray exposures Meyer and Rosi noted spontaneous resolution in 3 out of 4 cases of acute ileitis They controlled their observations by radiographic studies, in one case involving a child of 7 years of age, seven weeks after the exploratory operation the involved ileum appeared roentgenographically negative and free of disease Another case in an adult female was well one month after the operation radiographic examination revealed a normal terminal ileum An adult colored male was observed for 1½ years after exploratory operation for acute ileitis and was and remained radiographically negative for any residual signs of the previous inflammatory focus in the terminal ileum

In the series of Brown and Donald 7 out of 10 of the acute cases were well, 6 of them 3 or more years after the

simple exploratory operation The series of Warren and Sommers included 15 cases of acceptable acute ileitis 12 of these, or 80 per cent regressed, 2 progressed and one died McKinnon reported the spontaneous cure in a case of acute regional ileitis, 2½ years after the exploratory operation the patient was well and the radiographic examination, which previously had shown involvement of the terminal ileum, was now entirely negative

In the literature, the percentage of spontaneous resolution is considerably higher than in my present series Thus table 16 shows resolution in 33 out of the 59 cases collected from the current publications One may honestly question the validity of the follow up in some of these published cases Quite obviously, many of the reported cases had only recently been observed and often blanket statements are made as to complete resolution without adequate control by radiographic study and long period observation Nevertheless, the subsidence and complete cure of acute ileitis is convincingly shown by most of the cases in the reported literature, thus, Meyer and Rosi in a follow up of 1 month, 7 weeks and 1½ years, Brown 2 years 3 years and 4 years Bisgard and Hencke 2 years Rixford in discussing a paper by Mixter cites a case which had remained well for 8 years after an exploratory operation In the series reported by Eliason and Johnson 4 cases have remained well for 2 to 6 years 4 additional cases for not less than 1 year One case by Smithy was well 6 years after exploration the second case showed some radiographic evidence of the disease 6 weeks after exploratory operation but was well with a negative x ray examination 15 months later In Lehman's series of 7 cases, 4 have been free of symptoms of the disease from 14 months to 9½ years after the exploratory operation Kross followed his one case for seven years of complete restitution Lugh reports 2 cases of acute ileitis with spontaneous recovery One case was operated upon and acute terminal ileitis observed, 6 months later the case was reoperated and scarcely any evidence of the original lesion

was found. In the second case, after an operation for acute ileitis, the patient was followed by repeated x-ray examination until a completely normal bowel was observed roentgenographically. Probstein and Gruenfeld described acute ileitis of terminal ileum with severe hemorrhage, enterostomy. Three months later, at closing of the fistula, the *process appeared healed. A small section of the previously* involved ileum was removed for biopsy; the microscopic sections revealed only slight round cell infiltration of the subserosa. In a second case, only an enterostomy was performed for severe terminal ileitis (15 cm.). Two years later the patient was entirely well.

It is presumed in the literature that all those cases which did not advance to spontaneous healing gradually developed into instances of chronic regional ileitis. Meyer and Rosi make the point that when the mesentery is involved, spontaneous resolution is less likely to occur. The experience of Lehman, however, contradicts this opinion since in 1 of his cases with involvement of the mesentery, spontaneous resolution did occur; in another, with no mesenteric involvement, the after course was one of chronic regional ileitis.

(c) *The Medical or Surgical Treatment of Acute Ileitis*

The medical treatment of acute ileitis consists of the administration of a low residue diet, sulfasuxidine or sulfathaladine, over a long period of time, supplemented by the use of streptomycin. The efficacy of these antibiotics in effecting the cure may be questioned, since therapeutic conviction is not possible in the presence of a disease that shows ability spontaneously to resolve. The sulfa drugs may be continued indefinitely without danger; streptomycin 2 grams daily by intramuscular injection, supplemented by 1 gram per os, is certainly worth a trial. *In many cases of* acute fulminating ulcerative colitis, the value of streptomycin therapy is often strikingly convincing.

The surgical therapy at the time of the exploratory operation resolves itself into three possible courses of action

(1) Simple closure of the abdomen (2) Appendectomy alone closure of abdomen without drainage (3) A radical procedure (resection or short circuiting)

1 Where the preoperative diagnosis can be made with any sense of assurance such as the presence of diarrhea or a possible previous history of diarrhea, fever, or a rectal fistula, under such circumstances no exploration is justified In the absence of vomiting or rebound tenderness or of a mass, with low fever and a low leukocyte count, exploratory operation should be avoided If operation is undertaken under a false diagnosis simple closure of the abdomen without drainage is advocated

2 If, however the abdomen is opened and the exploration reveals an acute ileitis, shall the appendix be removed? There seems little justification for the removal of an appendix Though the practice of appendectomy is common under such circumstances, the pathologic report if scrutinized is invariably either negative or that of 'chronic inflammation' Ileitis does not affect the appendix, an organ which is attached to and constitutes a vestigial prolongation of the cecum the cecum is free of disease in all but exceptional combined types of the disease The appendix is affected only when involved in a large inflammatory mass of loops of ileum or in an abscess derived from a localized perforation of ileum This does not constitute acute appendicitis and does not call for appendectomy It is questionable whether the removal of the appendix is a disadvantage that leads to abdominal wall fistula In our series of 16 cases of acute ileitis 9 cases underwent exploratory operation in 3 instances the appendix was not removed with no fistula resulting In 6 instances the appendix was removed in 3 of which abdominal wall fistulas were noted as a sequel. Fortunately, 2 of the 3 fistulas healed spontaneously

Certainly, the removal of the appendix has no curative value as to the course of the disease Mixter advised against appendectomy Flinson and Johnson favor appen

dectomy only if the cecum and appendix seem to be involved in the pathologic process In their series of 15 cases, the *appendix was removed in all, yet but one fistula resulted* Drainage of the abdominal wound seems unnecessary and tends to fistula formation Smithy feels that appendectomy is purely incidental, does not increase the risk of fistula formation, he feels that to neglect appendectomy may invite later involvement of the appendix in the pathologic process with eventual development of acute suppurative appendicitis

My own experience does not favor appendectomy at the time of exploration, because such a procedure is unnecessarily superflous and tends to fistula formation Acute gangrenous appendicitis as a complication of chronic regional ileitis occurred subsequently only twice in this series of 222 cases

3 Is a radical procedure, such as resection or a short circuiting operation ever indicated at the time of exploration? The earlier surgeons with experience in this field, often advocated radical resection at the time of exploration Mixter was one of these earlier advocates of such a procedure, though his mortality was extremely high Jackman reported 2 cases of acute ileitis with resection at the time of exploration both patients recovering Harris reported what he thought was the earliest acute stage of regional enteritis in a female child, aged 5 years, with a short history of 3½ days Resection was accomplished without complications or shock and resulted in cure Probstein and Gruenfeld performed simple enterostomy in 2 cases of acute ileitis, with recovery in both instances as observed in the later examinations

Since the establishment of the fact that spontaneous healing was not only possible but likely in a large percentage of cases of acute ileitis, the consensus favors expectant waiting and noninterference (Koster et al, Brown, Mailer Eliason and Johnson, Smithy, Waugh, Meyer and Rosi)

That resection or a short circuiting procedure may even

tually become necessary is evident in the follow up of cases of acute ileitis In our own series of 16 cases, 4 were eventually subjected to ileo transverse colostomy one to resection of the chronic lesion, 4 cases are well along in the chronic phase but have as yet not consented to operation because of long periods of remission with freedom from symptoms The necessity for later operation has been noted by many of the current writers (Meyer and Rosi Eliason and Johnson Ebrill), and is a logical sequel to the chronic granulomatous phase of the disease

13 Ileo-Jejunitis

ILEO JEJUNITIS may be defined as that form or type of chronic enteritis in which the granulomatous process typical of that disease involves the jejunum either as an extension from the ileum or as independent lesion limited to the upper segments of the small bowel

Very soon after the original publication in 1932 of regional or terminal ileitis, it was recognized by Harris, Bell and Brunn that the upper ileum and the jejunum could be and were also involved in an almost identical pathologic process The literature, year by year, has added new case histories most of them on the regional form of jejunitis As early as 1934, Brown, Bargen and Weber reported 3 cases of enteritis with the lesion restricted to the jejunum In 1936 Meyer and Rosi mentioned a case with the inflammatory process localized in the jejunum In 1937 Pemberton and Brown already noted that 3 of 37 cases of regional enteritis were entirely restricted to localized segments of the jejunum Likely and Lisa reported in detail 2 cases of high jejunitis, resected, ending fatally and carefully studied at autopsy These were both localized lesions high in the jejunum and causing clinical intestinal obstruction Ravdin and Johnston in 1939 cited 16 cases of sole involvement of the jejunum in cases culled from the literature

In 1941 Crohn and Yunich published an analysis of 17 cases of diffuse ileo jejunitis with a clinical analysis of the outstanding symptoms and the therapeutic approach to the problem The differentiation of ileo jejunitis from

sprue was particularly emphasized Sussman and Wachtel added the distinguishing roentgenographic features in an analysis of 23 cases of granulomatous jejuno ileitis

Jejunitis or ileo jejunitis is not a separate or different disease, in all of its major characteristics it is but a sub

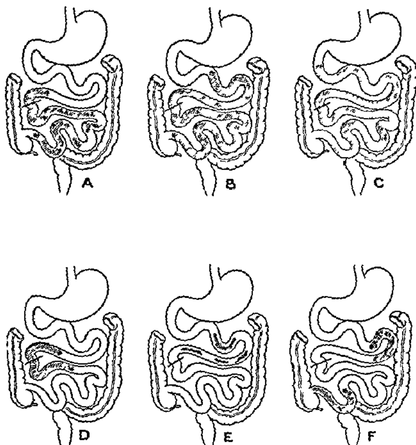


Fig 46—Distribution of Granulomatous Lesion in Ileo-Jejunitis (38 Cases) (A) Ileum and lower jejunum (cases) (B) diffuse ileum and jejunum (2_ cases) (C) diffuse ileo jejunitis with involvement of duodenum (2 cases) (D) upper ileum and lower jejunum (6 cases) (E) localized jejunitis (3 cases) (F) terminal ileum and upper jejunum (3 cases) Group B represents the greatest number of cases

type of the more common form of regional ileitis In its pathology as a granulomatous lesion, it is in no major way different from ileitis except in its anatomic distribution, one notes the same clinical characteristics, fever, diar



Fig 47—Terminal Ileitis and Jejunitis by Continuous Involvement in a 21 Year old Man Conservative medical therapy over a course of four years

rhea, a mass by palpation fistulas, rectal complications, anemia But the degrees of involvement are different the pathologic process is spread over a wider area, the local intensity is less marked in any one segment fistulas and rectal complications are fewer But the general constitutional disturbance is greater nutritional absorption is markedly impaired fever the enlarged spleen, the club

bing of the fingers indicate the degree of absorption of the toxic products of the disease skeletal growth is impaired Hypoproteinemia is a characteristic of the advanced pathologic state



Fig 48—Involvement of Lower Jejunum and Upper Ileum At onset gross hemorrhage melena diarrhea and continuous fever

The course is low grade often less severe a considerable degree of spontaneous healing is possible the disease is less amenable to surgical therapy than is terminal or regional ileitis

Ileo jejunitis should be considered and studied in its various forms in its anatomic and pathologic variations as illustrated in the 28 cases of ileo jejunitis which constitutes the present series (fig 46)

1 As an extension upward of an etiologically older process in the ileum

2 As a diffuse primary ileo jejunitis involving all of the ileum and the jejunum in its original distribution

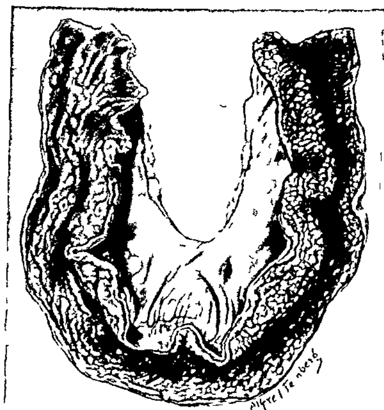


Fig 49—Pathologic Involvement of Upper Ileum and Jejunum

3 As constituted solely by a localized involvement of the jejunum in whole or in part

4 As isolated jejunal involvement plus another isolated segment of involved ileum the two processes being entirely discontinuous

1 *Involvement of the Jejunum by Upward Extension from a Chronologically Older Process of Regional Ileitis*

The usual form of this type is one of older terminal or regional ileitis in which by skip lesions or by continuous

extension the jejunum partakes of the same process which had originated in the lower ileum Only 2 of the 36 cases in this series illustrate this type of extension, the older process chronologically resides in the terminal ileum (fig 47) In these cases the severity of the process is so great that either initially or in the course of time the process of disease extends upward to involve the whole ileum and some of the lower jejunum usually as a continuous process (fig 48) Jejunitis as a complication of ileitis is also seen after unsuccessful surgical procedures in which repeated recurrences take place Following a resection or a short circuiting of the initial terminal ileitis a recurrence takes place in the new terminal segment of ileum Another resection is carried out followed by a new recurrence A third resection may occasionally be attempted any further recurrences may now carry the process up into the jejunum for the sacrifice of involved recurrent ileum may necessitate the resection of a wider area until the whole ileum has been dispensed with and the jejunum is invaded by the malignant extension of the disease process

2 *As Diffuse Ileo jejunitis*

This is the most common form seen and is constituted by a group of 24 of the total 38 cases under study Here the whole ileum and the whole or most of the jejunum are involved in a continuous process Occasionally, in the uppermost jejunum, the process is interrupted by the appearance of skip lesions separated by skipped areas of normal mucosa the lower jejunum and the whole ileum being the seat of one continuous process of disease (fig 49) In 2 of these cases the duodenum fourth and third portions were also involved by extension as seen radiologically and at operation

Chronologically it is impossible to determine which segment is the primary seat of the disease In practically all of this group the disease had universally involved the whole of the small bowel when first recognized so that it was impossible to state whether the initial process was in

the upper jejunum or in the lower ileum (fig 50) Presumably, in this severer type, the whole small bowel is

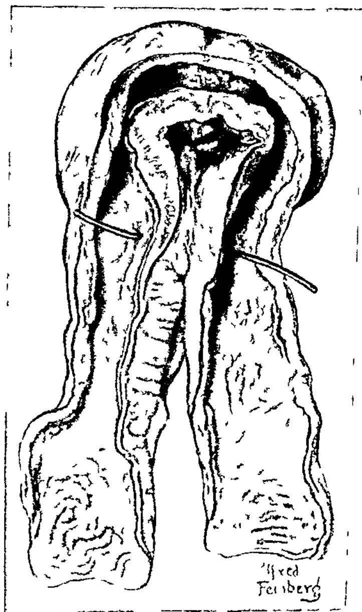


Fig 50—Pathologic Lesion Involving Lower Jejunum Fistula between loops of small intestine

simultaneously involved Twice, by radiologic examination, the stomach was suspected of participating in the process, but such involvement was never proven by either gastroscopy or by exploratory operation Barbour and Stokes in 1936 described a case which at autopsy was shown to have 13 areas of alternate thickening and thinning of the

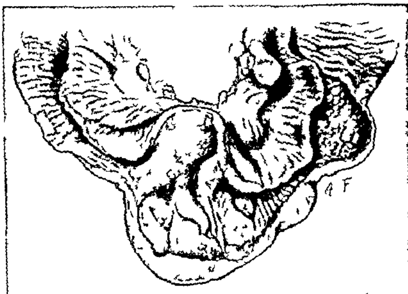


Fig 51 —Localized Jejunitis Occupying Uppermost Area of Jejunum Alternate constrictions and dilation enlarged mesenteric lymph node Characteristic cobblestone appearance identical with that seen in the terminal form of ileitis

entire small intestine from pylorus to the ileo cecal valve Holloway's Case 5 showed definite involvement of the third part of the duodenum as well as the terminal ileum and intermediate segments Rees has described the case of a 30 year old Negress who at operation presented the picture of multiple intestinal obstruction at three points in the upper jejunum due to segmental jejunitis resection en masse was surgically successful

3 *As Isolated Jejunitis*

This form is constituted by 9 of the total 78 cases in the

the upper jejunum or in the lower ileum (fig 50) Presumably, in this severer type, the whole small bowel is



Fig 50—Pathologic Lesion Involving Lower Jejunum Fistula between loops of small intestine

the duodenum was involved in this instance In a second case the terminal duodenum and 18 inches of proximal jejunum showed "thickened and beefy walls", here gastro jejunostomy was performed In the third case, 2½ feet of the proximal jejunum showed, on exploration, chronic inflammatory changes, again, gastro jejunostomy was performed Cases of primary regional enteritis involving the jejunum following trauma were reported by Browne and McHardy and by Spellberg and Gray

4 *The Combination of Isolated Jejunitis Plus an Isolated Segment of Ileitis (3 cases)*

In this type one notes two widely separated and discontinuous lesions, one in the upper jejunum as a sole lesion occupying 8 to 10 inches of jejunum, then far down usually in the terminal ileum is seen another separate and independent lesion of ileitis, the intervening mucosal area being free of extensions or of skip lesions In a case of W E Ladd cited by Homans and Hass a child had two diseased loops of small intestine, one in the jejunum and the other in the distal ileum (1933) Corr and Boeck as early as 1934 published a case of ileitis of 6 years duration, the ileitis beginning 3 feet above the ileo cecal valve A second lesion high in the jejunum was also present the whole picture being complicated by a recto vaginal fistula It is again impossible chronologically to state the relationship in time or in sequence between these two areas since they were both present when the diagnosis was first established Presumably both areas of disease were present from the initial onset of the pathologic process for from our study of regional ileitis it would be deduced that were the higher lesion an extension of the older process in the terminal ileum intervening skip lesions would have been observed This viewpoint is the logical deduction which follows from the study of the life cycle and the methods of extension of chronic regional ileitis

These variable segments of involvement in ileo jejunitis either as continuous, as isolated areas or as combination

group In 3 of them, *isolated areas of jejunum solely* were the seat of the disease, one was 4 inches, one 2 feet and one 4 feet from the fossa of Treitz, *a small isolated segment* of jejunum 6 to 8 inches in length being the seat of the pathologic process (figs 51 and 52) In the other 6 cases,

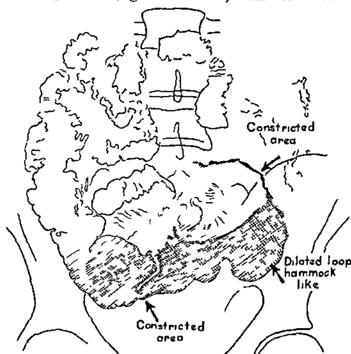


Fig 52—Localized Jejunitis Hammock like dilation between two areas of constriction Successful resection See figure 50 representing resected specimen

the lower jejunum was alone involved but the process was observed to extend also into the uppermost segment of the ileum

Instances of isolated jejunitis have been published by Johnson, by Brewster, by Gendel and Beaver, by Koenig, and by Lyons and Garlock James recently published 3 cases of regional jejunitis of unusual interest In one case, the whole jejunum from duodenum to ileum was involved *An anastomosis was made between the stomach* and the upper ileum in order to short circuit the lesion,

No new or significant factors as to the causation of ileo jejunitis are known as distinct from regional ileitis The same fundamental ignorance as to causation and etiology which covers ileitis applies also negatively to ileo jejunitis In none of the 36 cases in the group which forms the basis of this study was physical trauma attributed as a causative factor Trauma, however, has exceptionally been recited in the literature (Browne and McHardy, Spellberg and Gray)

Pathology

The pathology of ileo jejunitis differs but little from that of regional ileitis Grossly the small intestine is bluish red in appearance the serosa streaked by inflamed lymphatics The wall is thickened, coarse and firm, where long standing healing has taken place the lumen may be con tracted and the wall of the gut puckered On opening the resected specimen the mucosa is cobble stone in appearance as seen in ileitis cross hatching of longitudinal and trans verse ulcerations creating that appearance The mucosa is thrown up and prominent in places appearing as and even assuming a polypoid excrescent form True inflam matory polyps occur frequently and can be visualized in the roentgenograms The ulcers in the mucosa penetrate to the inflamed thickened submucosa these ulcers rarely penetrate more deeply and do not with rare exception form fistulous tracts The whole wall submucosa mus cularis and serosa is involved in the granulomatous and cicatricial process as evidenced by thickening edema con gestion Since much healing is capable in the upper small bowel, areas of contraction, moderate or extreme may appear with intervening dilated and distended loops of intermediate bowel (fig 53) Where two or more areas of constriction occur the intermediate bowel may be much distended *This over distended loop may give rise to ne* crosis of the bowel wall with abscess formation Or a perijejunal abscess may form in the thickened and inflamed mesentery the abscess being walled off and localized When

types constitute the various forms in which the disease occurs. The symptoms, the physical signs, the complications are more or less the same in all the forms; the radiologic study constitutes a means for the identification and recognition of the anatomic distribution, as checked against the findings at the exploratory laparotomy where such a surgical confirmatory procedure has been invoked.

Etiology

In this series of 36 cases, 11 were females, 27 were males, indicating a preponderance of male involvement of almost 3 to 1. It is possible that the series is too small to allow of a scientifically accurate conclusion, but throughout the series the major involvement of males is a striking characteristic. (In regional ileitis the proportion of males to females is 5 to 4.) Sussman and Wachtel found a similar incidence of 3 males to 1 female.

The age incidence in this series is striking as indicating a preponderance of involvement in the earlier decades of life (table 17).

TABLE 17.—*Ileo-Jejunitis: Age Incidence*

Age at onset Years	*No. of Cases*
1–10	1
10–20	17
20–30	9
30–40	7
40–50	1
50–60	1
60–70	0
Total	36 cases

The main brunt of the disease seems to fall in the second decade of life, the third and the fourth decades together contributing an almost equal number. After the age of 40, only a rare exceptional case is seen. The extreme youth of most of these cases of ileo-jejunitis is a striking fact. In the series of 23 cases of granulomatous jejuno-ileitis published by Sussman and Wachtel, the average age incidence was 27.0 years, the range varying from 9 years to 65 years of age.

of the adjoined mesentery, the subacute stage by a granular and hypertrophic mucosa containing punched out ulcerations with smooth or irregular edges the ulcers being either longitudinal or transverse to the axis of the bowel early polypoid proliferation and evident skip lesions are discernible The chronic stage is characterized by thickening *and fibrosis alternating areas of atrophic and hypertrophic* mucosa, multiple areas of stenosis the serosa being covered by a shaggy exudate This description includes the findings at four autopsies and the intestinal biopsies obtained at three of eight exploratory laparotomies and represents an accurate and painstaking study of the pathologic changes in the three various phases of the disease

Several forms of isolated jejunal ulcers appear in the literature, though there is some question as to the identity of such ulcers with the granulomatous forms which are recognized as ileo jejunitis Richardson in 1922 was responsible for the first American description he cited 2 cases of jejunal ulcer with stricture and perforation Buckstein gave a good description of primary ulcer of the jejunum Robinson and Wise in 1940 reviewed the whole literature and culled the large number of 36 cases of solitary ulcers *of the small bowel of which 7 were jejunal* Dowdle adds a case of multiple primary nonspecific jejunal ulcers with duodenal dilatation the bowel was obstructed not much below the ligament of Treitz with dilatation and thickening of the intestine above the strictured area

Symptomatology

An acute form of ileo jejunitis or phlegmonous jejunitis occurs in the literature though personally I have never seen such a case An excellent description is given by Clark and Wright of 2 personally observed cases of acute phlegmonous enteritis the first case was characterized by an acute onset a mass in the left upper quadrant of the abdomen high fever leukocytosis it terminated in death At autopsy an area of acute jejunitis was seen 30 cm from the pylorus and extending distally for 20 cm In the

such an abscess forms, it may become adherent to the ab dominal wall at the site of the scar of a previous incision and discharge its content Fecal fistulas to the abdominal wall are, however, rare The lymph nodes of the mesentery are enlarged and succulent, similar to those seen in distal terminal ileitis Microscopically, the process is identical with that of ileitis and of intestinal granulomata in gen



Fig 53—Diffuse Ileo Jejunitis with Major Involvement of Jejunum Alternating areas of constriction and dilation scattered throughout the small intestine Marked hypoproteinemia severe diarrhea, progressive loss of weight Prognosis is poor

eral Miliary like tubercles consisting of lymphoid and epithelioid mononuclear and plasma cells are common and *frequently enclose giant cells presumably of foreign body nature* The lymphoid follicles are hyperplastic with active germinal centers In their excellent article, Sussman and Wachtel describe the pathology as well as the radiologic appearance of the disease as occurring in three stages namely acute, subacute and chronic The acute stage is characterized by edema and thickening of the mucosa and

of the adjoined mesentery, the subacute stage by a granular and hypertrophic mucosa containing punched out ulcerations with smooth or irregular edges, the ulcers being either longitudinal or transverse to the axis of the bowel, early polypoid proliferation and evident "skip lesions" are discernible The chronic stage is characterized by thickening and fibrosis, alternating areas of atrophic and hypertrophic mucosa, multiple areas of stenosis, the serosa being covered by a shaggy exudate This description includes the findings at four autopsies and the intestinal biopsies obtained at three of eight exploratory laparotomies and represents an accurate and painstaking study of the pathologic changes in the three various phases of the disease

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fever, (b) diarrhea, (c) severe abdominal pain, (d) gross hemorrhage, (e) symptoms of obstruction, (f) anorexia, (g) loss of weight, (h) anemia

Fever was present in 17 of the 36 cases in this series, the fever is intermittent in type, higher in the late afternoon or evening, may rise to 103 F, though usually the range is between 100 and 102 F temperature, chills are occasionally noted The fever may be so mild as to be almost imperceptible and may not be accompanied by malaise or prostration The fever may be paroxysmal remaining continuously for several weeks or months, or may be interrupted by periods of apyrexia

Diarrhea is the most constant symptom, occurring in 31 of the 36 cases in this series, constipation is noted once only, normal bowel movements in the remaining four instances The diarrhea is never extreme, averaging usually two to four movements per twenty four hours The stools are mushy or semisolid, mixed with thin mucus, occasionally watery Pus is never seen, gross blood in flecks only exceptionally The guaiac reaction was positive in 10 cases, negative in the remainder In fact, it is not unusual to have negative guaiac reactions in the feces of proven cases throughout the course of the disease

Abdominal pain is another almost constant symptom, having occurred in 30 of the 36 cases in this group The abdominal pains are crampy in nature, diffused over the abdomen, or more likely to be localized over the left upper quadrant The pains may be mild and associated with the desire to defecate or severe and definitely pre defecatory in timing With the passage of fluid feces and gas accompanied by an audible gurgling the cramp is allayed When obstructive phenomena are present, the abdominal cramps are more or most severe occasionally accompanied by vomiting

Gross hemorrhage occurred once in this present series In a previously studied series it occurred three times as an initial symptom out of 17 observed cases The gross

second case, the acute lesion was 50 cm above the ileo cecal valve in the upper ileum, the area involved again extending for 20 cm into the jejunum They reviewed the literature and cite 12 cases in the duodenum or proximal jejunum, 22 cases in the jejunum alone, and 7 in the ileum, many of which, however, resembled granulomata and were associated with foreign bodies, fish bones and diverticula

Very recently, Husebye presented 14 cases of acute phlegmonous jejunitis as seen by x ray, in six instances the diagnosis rested essentially on the roentgen appearance of the films, seven of the fourteen patients recovered The roentgen findings were characteristic and consisted of (1) Reduced diaphragmatic movements on one or both sides (2) Scout films revealed distended loops of gut over the left abdomen (3) Erect films revealed fluid levels (4) By barium meal, the mucosal relief was roughly jagged with irregular circular folds partly sharp and partly blunt

Apparently, this form of acute phlegmonous jejunitis is an extremely severe one with a high mortality and with grave symptomatology Involvement of the duodenum as part of a high jejunitis has recently been described by James in 2 out of 3 cases In one case, the process involved the distal duodenum and the whole of the jejunum In a second case, the process involved the terminal duodenum and 18 inches of the upper jejunum, the duodenum just at the fossa of Treitz being kinked and adherent to the loop of jejunum

The classic form of chronic ileo jejunitis or jejunitis is that of a low grade granulomatous inflammatory lesion, involving primarily the jejunum either continuous with a similar process in the ileum or associated with an independent lesion in the distal ileum

The onset is usually gradual and prolonged, lasting from six months to fourteen years or more The actual onset is often difficult to estimate since the occasional slight diarrhea, mild fever or loss of weight is little noticeable

The outstanding clinical symptoms were (a) low grade

case, who had remained stunted in growth and devoid of secondary sex characteristics later recovered fully from the diffuse ileo jejunitis from which he had suffered, grew to be a strong well developed man married and was the father of two children

The menses are rarely skipped in ileitis as they are in severe ulcerative colitis Several cases of ileo jejunitis have married, borne normal children without detriment to their general health or difficulty, and without the induction of a recurrence of the disease process

Aphthous stomatitis (3 cases) furunculosis, erythema nodosum, epidermolysis bullosa were each seen once Phlyctenular conjunctivitis was twice seen Manifestations of hypovitaminosis are not often seen, occasionally, one notes bleeding gums glossitis as evidence of nicotinamide deficiency, riboflavin deficiency as marked by cheilosis though these are extremely rare Vitamin A deficiencies night blindness, the bone changes of vitamin D deficiency have *not been noted*

Killian and Ingelfinger studied the nutritional problems presented by a patient with extensive ileo jejunitis A 23 year old boy with a previous history of a loss of 40 pounds of weight was torpedoed during the recent war and was exposed in a life raft for eight days He was found in a state of extreme malnutrition emaciated dehydrated with pitting edema of the lower extremities The tongue was smooth, fever up to 102 F, hemoglobin 54 per cent, red blood cells 1 200 000 hematocrit 22 per cent Serum protein was markedly reduced to 4 85 grams per 100 cc albumin 2 34 globulin 2 51 grams per cent Clubbing of the fingers was present, the glucose tolerance test showed hypoglycemia with a low tolerance curve By x ray examination the lower jejunum and the ileum showed marked irregularities and points of narrowing with localized dilatation and constricting Serum calcium was 8 0 and 8 2 milligrams per cent Inorganic phosphorus 2 5 and 3 8 milligrams Vitamin A absorption of 200,000 U S P units was only slightly below normal

hemorrhage takes the form of melena, though once it was accompanied by a brisk hematemesis The hemorrhage while profuse is never exsanguinating, and usually not associated with shock

Symptoms of obstruction are frequent and occurred in a mild form in 10 of the 36 cases The intestinal obstruction is of low grade, none of the cases of this or of our previous series of 17 cases, having come to operation because of advanced obstructive symptoms The obstruction is usually inflammatory in nature and is due to edema of the bowel wall, possibly accompanied by a perijejunal or a mesenteric abscess and subsides as the inflammatory process recedes Vomiting was noted in 5 cases Browne and McHardy mention obstruction as one of the symptoms in their case of a Negro boy who developed a localized jejunitis following a severe abdominal trauma

Anorexia and weight loss are common manifestations The loss of appetite is spotty and occurs during acute exacerbations of the chronic process, at other times appetite may be well maintained

The weight loss may be very severe amounting in some of our cases to as much as 50 pounds in a stout girl The average loss of weight in our previous series was 17½ pounds During the healing phases, with remissions of the fever and diarrhea the weight may be rapidly regained, 15, 25, or even 50 pounds may be added during prolonged remissions of the symptoms

The *nutrition* is usually poor skin dry, mucous membranes pallid An extreme degree of malnutrition with inanition and loss of strength marks the end stages of lethal cases Retarded growth and retarded sex maturation are commonly observed in those young adolescents who are so frequently affected by the disease at a prepubertal age With the recovery from the severe phase, and with healing of the lesion advancing weight, growth in height, and secondary sex maturation may replace the hypogonadalism seen in the adolescent years One of our earlier

little from the normal, a very mild leukocytosis up to 8,000 to 10,000 or even 18,000 white blood cells may be noted though most usually the count is within the lower range of normal Eosinophilia as seen in ulcerative colitis is unusual, though it was seen in 5 patients of our previous series, up to 14 per cent of eosinophiles being present in the blood smears A mild secondary anemia was present in 12 out of the 36 cases in this series, the range being usually between 72 and 50 per cent hemoglobin (Sahli) A macrocytic hyperchromic type of anemia occurred once in our previous series, with a color index of 1 3 In this series of 36 cases hyperchromic anemia was not observed even though the anemia was at times severe and the intestinal absorption severly compromised as noted by hypoproteinemia The hyperchromic anemia in ileo jejunitis is usually not beneficially influenced by intramuscular injections of crude liver extract the reticulocyte response attaining a level of only 7 per cent this in contrast to its more successful therapeutic result in cases of nontropical sprue

The occurence of macrocytic anemia in association with intestinal lesions particularly intestinal strictures and anastomoses was amply demonstrated in the literature by Faber Hale White by Meulengracht and by Hurst Butt and Watkins mention 7 cases of diffuse ileitis with macrocytic anemia in 6 of which a fecal fistula co existed With proper reconstructive surgical intervention the macrocytic type of anemia could be returned to a normal blood picture They rightly ascribe the hyperchromic anemia to the abnormal interference with absorption and improper utilization of the effective hemopoetic fraction of the diet Plum and Warburg in a publication entitled Hematological Changes Especially Megalocytic Anemia in Regional Ileitis describe 4 cases under their personal observation in which the blood picture was typical of that of a hyperchromic anemia The hemoglobin values ranged as low as 20 per cent red blood cell count as low as 1 410 000 cells

levels, fasting serum carotene almost normal The patient improved rapidly under high protein diet and amino acid concentrates The intravenous administration of amino acids did not improve the nitrogen balance or create nitrogen retention in the metabolism studies

Loss of fat soluble vitamins was especially emphasized in *Albright and Stewart's report* The case, a woman aged 35 years had undergone four successive operations for ileitis and recurrent ileitis, including two extensive intestinal resections Protracted severe abdominal cramps and diarrhea resulted in tetany and a state of marked vitamin deficiency The prothrombin time was found to be only 13 per cent of normal, indicating a marked associated vitamin K deficiency Vitamin C was within normal range Fat soluble vitamin A was somewhat deficient 8 2 units per 100 cc of serum (normal 10–20 units) carotenoids somewhat diminished, and associated with a xeroderma of the breast and abdomen Fat soluble steroids, particularly the quantity of 17 keto steroids in the urine were practically absent The tetany responded rapidly to large doses of vitamin D, 500 000 USP units daily The results of treatment in the form of liberal dosage with all of the fat soluble vitamin preparations was clinically dramatic

An unusually exaggerated degree of hypoproteinemia was noted in a diffuse case of ileo jejunitis by Casten At a previous operation an anastomosis between the upper jejunum and the transverse colon had been performed because of a diffuse inflammatory process involving all of the ileum and the lower jejunum Extreme malnutrition and evidences of hypoproteinemia were soon evident The total serum proteins fell to 3 1 grams per 100 cc, the albumin fraction being 1 1 Gm and the globulin 2 Gm (albumen globulin ratio 0 55) Most observers conclude that the critical level of serum protein is 5 0 Gm per 100 cc, edema will invariably result when the blood level falls below that point

Blood changes The white cell count varies only a

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Blood changes The white cell count varies only a

wall occurred only once in this series Internal fistula, jejunal to ileum, was once observed radiographically

In cases of localized intestinal obstruction the whole abdomen may be distended visible peristalsis was not seen since the degree of obstruction is not complete The edge of the spleen was palpable three times in this series clubbing of the fingers was observed twelve times in this series of 36 cases Clubbing of the fingers is a significant observation and indicates the degree of constitutional alteration invoked by so diffuse an intestinal process (fig 54)



Fig 54—Clubbing of the Fingers in a Case of Diffuse Ileo Jejunitis Massive involvement of the whole jejunum and upper ileum palpable spleen

color index 1 12, 1 19, 1 15, 1 05 at the point of greatest severity In one case the jejunum seemed definitely to be involved Barker and Hummel similarly quote a case of ileitis with resection and a secondary short circuiting operation and a consequent hyperchromic anemia

Sprue, a disease without noticeable organic changes in the intestinal mucosa, but with completely deficient intestinal absorption is often characterized by a hyperchromic or macrocytic type of anemia Ileo jejunitis, by contrast, is a disease with extensive organic destruction of wide areas of intestinal mucosa, yet absorption is better maintained in spite of severe and extensive ulcerations and a hyperchromic type of anemia is rare

The erythrocytic sedimentation rate may be somewhat accelerated, as seen in 5 patients The total blood protein of the plasma is appreciably diminished in the more severe cases (5 8 Gm), reaching a minimum of 4 0, 4 4, and 4 5 grams per 100 cc in 3 cases and as low as 3 8 grams in a very severe case of ileo jejunitis The albumin globulin ratio is disturbed approaching a ratio of one but rarely completely reversed

The urea, phosphorous blood chlorides and blood sugar are but slightly if at all lowered The blood calcium may be materially reduced, 2 of the patients in our present series having shown frank symptoms of tetany

Gastric analysis showed normal titrable acidity in all cases except one of achylia gastrica

The physical examination of a case of ileo jejunitis may not be noteworthy Some of the cases show well maintained nutrition, *others may give evidence of pallor and extreme* malnutrition in the later stages of a deteriorating status A mass is occasionally present (6 cases), usually in the *left upper abdomen and corresponds to the inflamed mesen*tery of the jejunum with the associated granulomatous loops of bowel Such a mass may *often be adherent to the* anterior abdominal wall forming a localized abscess requiring incision and drainage External fistula to the abdominal

tory operation The disorientation of the mucosal pattern of the jejunum and upper ileum is usually capable of recognition, segmentation and delayed puddling may occur similar to that seen in sprue, but in jejunitis there are frequently distended loops of bowel proximal to a localized partly



Fig 56—Diffuse Ileo Jejunitis in a B y 17 Years of Age Exploratory operations (two) Impossibility of surgical relief with rapid downward course

strictured area, or even evident skip areas separating involved segments of bowel (fig 55)

The roentgen findings in ileo jejunitis are well described by Sussman and Wachtel They were unable in the acute phase of the disease to differentiate jejunitis from sprue

Rectal complications do not occur with the same frequency as in regional ileitis. In this series perirectal fistulas were present four times, a perirectal abscess twice, rectal fistula once.

Roentgenographic Recognition of Ileo Jejunitis

The barium meal as utilized with reduced amount of



Fig. 55.—Ileo Jejunitis Involving Upper Ileum and Lower Jejunum Resection in continuity at the Mayo Clinic with brilliant result. Complete restoration of health.

barium sulphate and with frequent fluroscopic and film controls is the method of choice. The degree and extent of involvement of the jejunum and ileum are definable with great accuracy as checked against the findings at explora-

the barium rapid passage and poor mucosal pattern In the chronic phase of the disease, greater rigidity and irregularity were noted, the barium seemed to make a cast The



Fig 58—Same patient as in Figure 57 Radiograph taken two and a half years later during which time subsidence of symptoms and a gain of 50 pounds in weight were noted Observe by comparison the *increased lumen of the jejunum and ileum but persistent irregularity* in contour probably evidence of scarring Note also absence of stenosis or stricturing

rigid loops had a pipe stem appearance with occasional areas of dilatation multiple stenotic areas and occasionally evident polyposis was suggested (figs 56–58)

the same patchy segmentation was present in the loops of the bowel, the valvulae conniventes seemed further separated, the outlines of the jejunum were hazy The loops of intestine showed persistently increased activity with



Fig 57—Diffuse Ileo Jejunitis in a Woman 50 Years of Age Observed *over a Course of Several Years* Radiograph taken in 1935 at the height of the active process showing involvement of the whole ileum and lower jejunum See figure 58

lack of flexibility The terminal ileum was also involved in half of their cases

In the subacute phase, the jejunal loops showed more pronounced alteration in contour, uneven distribution of

the barium, rapid passage and poor mucosal pattern In the chronic phase of the disease, greater rigidity and irregularity were noted, the barium seemed to make a cast The



Fig 58—Same Patient as in Figure 57 Radiograph taken two and a half years later during which time subsidence of symptoms and a gain of 50 pounds in weight were noted Observe by comparison the increased lumen of the jejunum and ileum but persistent irregularity in contour probably evidence of scarring Note also absence of stenosis or stricturing

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Differential Diagnosis

The main point of interest lies in differentiating high ileo jejunitis from sprue and from the secondary vitamin deficiency manifestations Sprue is characterized by typical frothy and fatty stools, by a severe secondary anemia or by one of hyperchromic type with a high color index Fever is absent, the stools do not contain blood, gross



Fig 59—Sprue Characteristic Segmentation of Barium in Loops of Small Intestine Contrast ileo jejunitis in figure 60

hemorrhage either as melaena or as hematemesis is missing The sprue case reacts well and promptly to deep injections of crude liver extract and vitamin B complex with the evident reversal of the mucous membrane disturbance of pattern and an attempt at least partially to resume a normal mucosal mosaic The lower or terminal ileum is usually free of disease in sprue, but may often be involved in jejunitis The intermittent areas of constriction and large

dilatation which is present as obstructive phenomena in jejunitis are absent in sprue (figs 59 and 60)

In jejunitis, marked general clinical improvement may be noted as a result of general hygienic measures and the administration of liver extract and vitamins, but the diffuse string signs throughout the jejunum and ileum are irre



Fig 60 —*Linear Distribution of Barium in Ileo Jejunitis in Contrast to Sprue in Figure 59*

versible and remain permanent even though general good health and nutrition are restored In a case of diffuse ileo jejunitis observed over a course of 10 years, a complete subsidence of symptoms occurred with a regain of 50 pounds of weight The repeated x ray examinations revealed year after year the same continuous string signs occupying jejunum and ileum as seen at the time of the first observation Evidently permanent scarring and cicatrization of

the intestinal wall had occurred and persisted even though clinically the patient had been restored to good health

The absorptive capacity of the intestinal tract differs in sprue from that of ileo jejunitis In sprue, the oral glucose tolerance test gives flat curves consistent with poor or deficient intestinal absorption The same applies to tests for the intestinal absorption of vitamin A, as shown in experiments by Adlersberg In ileo jejunitis, the oral glucose tolerance test is more likely to approach the normal rise and fall as is also the absorption of vitamin A from the intestinal tract According to Adlersberg and Sabotka, ileo jejunitis and sprue can be reliably differentiated by postdigestive tests for the absorption of fats and vitamin A In the active stages of sprue there is complete inability of the intestine to absorb fat and fat soluble vitamin A during remissions, after adequate treatment, one observes fairly satisfactory absorption of both They studied 5 cases of diffuse ileo jejunitis The fasting lipids of the blood serum averaged 377 mg per cent in ileo jejunitis four hours after a fatty meal the blood serum lipids averaged 623 mg per cent a rise of 65 per cent, in contrast to sprue in which a rise of only 3 per cent was observed After feeding 90,000 to 180,000 I U of vitamin A, the level in the blood serum rose in ileo jejunitis from 63 I U per cent to 94 I U per cent, in contrast to active sprue where an actual loss was demonstrated

The vitamin deficiency states with disturbances of fat metabolism such as accompany severe ulcerative colitis, give roentgenographic changes similar to those of sprue and often to those of mild diffuse jejunitis They have been described by Snell and Camp, by Mackie and Pound, and by Adlersberg and Weingarten Mild puddling, delay in jejunal loops irregular outline of the upper ileum and lower jejunum, such as occur in sprue and in jejunitis may be present, there are no manifestations of delayed motility and no obstructive or polypoid changes in the roentgenograms

Hodgkin's disease of the small bowel and diffuse multicentric sarcomatosis of the mesenteric lymph nodes with intestinal involvement are rare diseases, which simulate jejunitis. Both of these diseases are extremely malignant, the course is rapid and downhill and perforation and hemorrhage not uncommon.

Continuous fever of intestinal origin arising in ileojejunitis or ileitis must be recognized in the differential diagnosis where more common diseases of febrile nature receive first presumptive consideration. Diseases characterized by continuous fever with low leukocyte counts include such *syndromes as brucellosis, rheumatic fever, periarteritis nodosa, lupus erythematosis disseminatus.* The advent of diarrhea so often overlooked or ignored indicates the possibility if not the likelihood of ileojejunitis as the true cause of the febrile state [69].

14 Ileo-Jejunitis—Treatment

Course and Prognosis

THE OUTLOOK in a case of ileo-jejunitis depends to a large extent upon the degree and type of involvement of the small bowel. Where diffuse ileo-jejunitis exists the prognosis differs materially from those cases in which localized or segmental involvement is exclusively present. In the localized form surgical resection or a short-circuiting operation becomes a profitable procedure. Progress of the disease from one segment of bowel to a higher or a lower level of intestine has not been observed in this series; on the other hand recession of the lesion with healing, though with persistent x-ray deformity of the bowel, is possible and has been observed.

In the former series of 17 cases previously published (Yunich and Crohn) 4 of 9 cases of diffuse ileo-jejunitis had done well without recourse to surgery, gained strength and weight. Five consecutively treated cases gained some weight, diarrhea diminished, anemia was overcome (fig. 61); the end result was less satisfactory.

In this series of 38 cases the end results were as shown in table 18 (follow-up two to twelve years).

TABLE 18.—*Ileo-Jejunitis: Follow-up in Present Series*

	Cases
Clinically well	[illegible]
Clinically fair	6
Poor with persistent symptoms	
Died	[illegible]
No follow-up	[illegible]

It will be noted that 13 of the 38 cases were clinically so improved and free of symptoms as to allow of the clinical impression of being restored to health In most of these cases, clinical improvement was not paralleled by changes in the roentgenograms However, a recent experience was

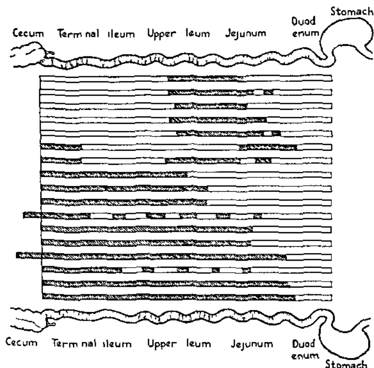


Fig 61 —Distribution of Anatomic Lesion in an Earlier Series of Cases Note the continuous forms of ileo jejunitis the extension forms the skip lesions and the purely localized forms of jejunitis

most illuminating Five years ago a patient was noted to have had diffuse involvement of the jejunum and upper ileum with active symptoms On returning this year for follow up observation marked clinical improvement was noted with cessation of all active symptoms On re x ray at this time the jejunal pattern was seen to be restored to normal the upper ileum was contracted and disarranged

thus indicating the greater susceptibility of the upper jejunum to self healing. Such instances of apparent cure of jejunitis, confirmed by exploratory operation or by roentgenography, have previously been independently noted by Pessagno, by Wilensky, by Sussman and Wachtel, and by Kross in individual cases.

On the other hand, the severity of the disease is indicated in the fact that in this series 6 cases were only fair, 7 were poor and, above all, 6 had fatal terminations. These deaths occurred as a result of brash surgical intervention (2 cases) or as a result of perforation, (1 case), of sepsis (Friedlander bacillus) (once), of inanition (1 case), of intercurrent disease 1 case. The unsatisfactory clinical outcome in 19 cases including 6 deaths is clear evidence of the severity and persistence of the disease process in progressively undermining nutrition and protein and mineral reserves.

The fact, however, that 13 cases did improve so as to resemble clinical cure, is impressive, and does indicate the fact that self healing in high jejunitis is possible. The regain of weight in these cases is impressive and the surcease from fever and diarrhea and anemia most striking. In the series of 23 cases published by Sussman and Wachtel, the end results were quite similar insofar as of 17 cases observed through a prolonged follow up 5 cases became inactive, 3 died postoperatively of intestinal obstruction, 3 continued in an active phase with exacerbations, 6 continued with chronic low grade activity. One case was followed to spontaneous regression and to the restoration of good health and function. From this publication one would gain the impression that the prognosis in ileo jejunitis is most unfavorable.

Medical Treatment

The conservative treatment of ileo jejunitis applies principally to the type in which diffuse involvement of the entire small bowel exists or to those in which the disease affects such large stretches of upper ileum and the whole

jejunum as to preclude any idea of surgical intervention The conservative approach to therapy is aimed at establishing some degree of partial sterilization of the intestinal tract by the use of antibiotics and to maintain nutrition and electrolytic balance in the plasma and to combat anemia and vitamin deficiencies

As antibiotics penicillin is useless streptomycin possibly of some avail In the febrile cases of ileo jejunitis, streptomycin in doses of 2 or 3 grams daily intramuscularly administered would seem well worth the trial The insoluble sulfonamides, sulfasuxidine and sulfathaladine in large dosage is regularly administered in this type of presumable intestinal infection Whether such sulfonamides have curative value, or merely act as inhibiting agents upon secondary infection remains to be determined Several patients have reported control of diarrhea and pain while taking the sulfonamides, with recurrence of the symptoms upon discontinuance of the oral sulfonamide therapy, in the main the specific therapeutic value of the sulfonamides by and large remains open to question

Nutrition is maintained by a liberal soft nonroughage or bland diet not too strictly construed High protein, high carbohydrate elements in the diet are stressed meats, fish, cheese, eggs milk, pureed vegetables, and fruit juices, bread and butter being forced (See page 116) The protein content of the diet may be reinforced by the use of the protein hydrolysates up to 4 to 6 ounces a day being urged upon the patient The newer commercial preparations are no longer bad tasting are actually palatable, and tend to maintain and restore nitrogen balance Occasional transfusions of whole blood or of plasma or the intravenous use of amino acid hydrolysates aid in overcoming hypoproteinemia, raise the total proteins of the blood and restore when plentifully administered over a long period of time the relationship between the albumin and globulin fractions of the serum

The intramuscular injection of crude liver extract plus vitamin B complex, 2 cc of each, every day or every other day, tends to overcome anemia, encourages blood formation and replaces the deficiency in vitamin absorption which results from the damaged intestinal tract Even though



Fig 62—Diffuse Ileo Jejunitis in a 28 Year Old Man Slowly progressive course episodic flare up of fever abdominal pain and diarrhea marked clubbing of fingers palpable spleen

the beneficial effects of such injections are not as evident in ileo jejunitis as in sprue they should continue to be regularly administered

The administration of folic acid by mouth is often to be recommended particularly in the types with hyperchromic forms of anemia

Fresh air, sunshine and much rest, particularly at the seashore or in the mountain air, often acts very beneficially to effect general improvement in weight and strength.

Surgical Intervention

The indications for surgical interference are limited to those cases in which the lesion is localized to one or more



Fig. 63.—Diffuse Ileo-Jejunitis in a Woman 28 Years of Age. Confirmed by Exploratory Laparotomy. Inoperable situation, subsequent multiple abdominal wall fistulas, rapid downhill course.

isolated segments of the small bowel such as the Group C or Group D of the original description. (See page 160.) Of the 36 cases in this group 18 were explored; in 7 only had an appendectomy been performed; 5 cases were subjected either to an intestinal resection or a short circuiting procedure. Surgical exploration is always warrantable and indicated where the true nature and extent of the disease is in some doubt. A case may seem to be segmental or localized in extent and at exploration may be discovered to be of the diffuse type. Or a case considered diffuse and

probably incapable of surgical help may be determined at exploratory operation to be segmental and capable of resection (figs 62–69)

Where no benefit is being derived by conservative medical treatment, an exploratory operation is often justified The removal of the appendix is a superfluous manipulation



Fig 64 —Diffuse Ileo Jejunitis in an 18 Year Old Girl Unsatisfactory clinical course progressive loss of nutrition hypoproteinemia

fortunately, in ileo jejunitis appendectomy rarely results in abdominal wall fistula

In Group A, where the disease is an extension upward of ileitis so as to invade and include the jejunum no radical surgical procedure offers much hope of success

In Group B, those cases in which the disease invades the whole of the jejunum and much or all of the ileum the same discouraging attitude toward reckless excision of the involved intestine holds equally true

Massive resections of the small bowel with the sacrifice of most of its length has been occasionally encountered in

the literature, not for ileitis or jejunitis, but more often for strangulation for volvulus for superior mesenteric vein thrombosis or for intussusception The average length



Fig 65—Diffuse Ileo Jejunitis in a Man 48 Years of Age Note multiple areas of constriction chronic course Episode of fever abdominal pain and obstructive phenomena In the interval between attacks preserved well being good nourishment and active working efficiency

of the small intestine varies under normal conditions from 18 to 26 feet averaging 21 feet 6 inches

Gray s Anatomy	20 feet 6 inches
Rost	*18 to 26 feet averaging 19 feet*
Treves	22½ feet in the male
	23¼ feet in the female adult

Sunoff felt that half of the small intestine could be sacrificed without unduly endangering life and quoted 5 cases in which 18, 17½, 17, 16, and 13¼ feet of small bowel had been removed all survived the operation, but died later

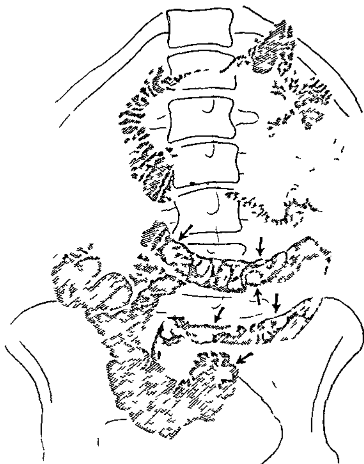


Fig 66—Diffuse Ileo Jejunitis Polypoid Formation throughout Upper Ileum Patient maintained good nutrition and weight no evidence of anemia normal blood figure He leads a normal life actively efficient

Pate reported a case in which 12½ feet of small bowel were removed for a traumatic strangulation of the mesentery, only 12 inches of jejunum remaining, the patient was well four weeks later In a case reported in 1940 (Todd, Dittenbrandt and Montague) all but 3 feet of jeju

num had been surgically removed, resultant carbohydrate metabolism was normal, proteins not so well absorbed (67, 75, and 76 per cent in three periods) tetany was prevented by liberal administration of calcium and Vitamin D In their study of the metabolism in their case, 25 per cent of the protein intake and 45 per cent of the fat intake

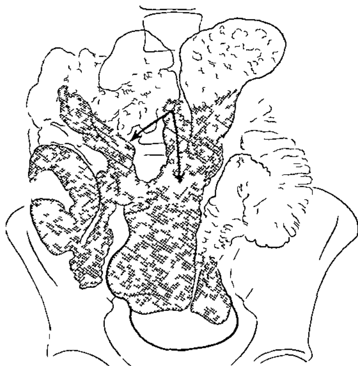


Fig 67—Diffuse Ileo Jejunitis Involving Upper Ileum and Lower Jejunum

were lost in the feces a total loss of 25 per cent of the calorific value of the ingested food The fecal fat showed much free fatty acids indicating good splitting but poor absorption

Coleman and Bennett report massive small intestinal resection with survival the resection involving 6 feet 7 inches in one case 14 feet 8 inches of small bowel in another

case Prioleau also supports the view that massive resection of the small intestine is possible with survival under fortunate circumstances He reports 2 cases, one with a 40 per cent resection and one with a 53 per cent resection of the small bowel with survival, though the latter case died four months later Elman and Reed report the

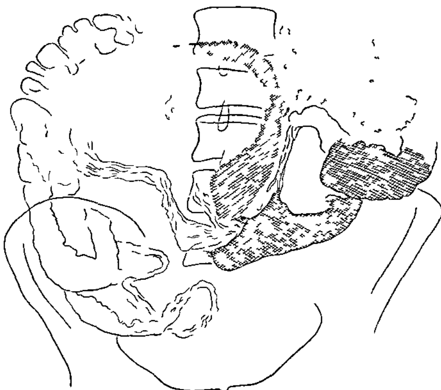


Fig 68 —Diffuse Ileo Jejunitis

resection of all but 3 feet of proximal jejunum and also the right half of the colon the patient gained 50 pounds of weight and experienced normal bowel function The results of human resections indicate that approximately two thirds of the small bowel can be removed without serious risk to life (Berman et al) They report the removal of all but 18 inches of the jejunum and the right half of the colon for ergot poisoning and superior mesenteric vein thrombosis with complete recovery the daily postoperative defecations

were limited to three formed stools per twenty four hours At the 1948 meeting of the American Gastroenterological Association Althausen reported the resection for mesenteric thrombosis of 435 cm of small intestine, including the

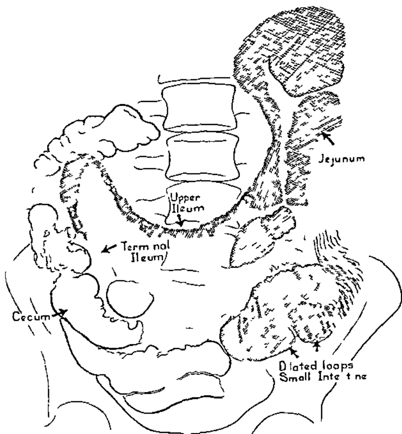


Fig 69 —Diffuse Ileo-Jejunitis Involving All of Ileum and Most of Jejunum

entire ileum and all but 15 cm of the jejunum The patient survived the operation tolerably well with retained nutrition as proven by extensive studies of metabolism and of food absorption

While such massive resections of small bowel are thus

shown to be possible, with survival, the attempt to apply that principle to diffuse ileo-jejunitis would likely be associated with an extremely high mortality because of the previous state of malnutrition and anemia, and is scarcely to be encouraged.

In Group C, those cases with high and isolated segmental involvement of the jejunum, localized resection of the lesion is not only possible but is highly successful. Such was the outcome in our 3 cases in this present series. Johnson resected 3 feet of upper jejunum beginning at the fossa of Treitz for localized jejunitis. Brewster resected 2 feet of jejunum for a lesion beginning 2½ feet caudad of the fossa of Treitz. Both cases made complete recoveries. Spellberg and Gray performed a gastroenterostomy for a traumatic *segmental jejunitis*, *because of poor result denoted* by delay in the proximal loop, a secondary resection was performed with a successful outcome. Gendel and Beaver had an identical experience. Lyons and Garlock resected 10 inches of upper jejunum for localized jejunitis, whose upper limit was the fossa of Treitz, with good result. The case of Koenig was equally successful after a resection of 3 feet of jejunum.

In high jejunitis multiple segments of involvement are not uncommon. It often becomes necessary to treat or resect each individual focus of disease as an independent lesion, in order to achieve a successful outcome. Dixon cites a striking case of recurring obstruction *from multiple* non-neoplastic tumefaction of the jejunum. An interesting insight into the life history of localized jejunitis may be gained from the study of a case recently published by Husebye. In 1928 a 49-year-old man was operated upon for an acute phlegmonous jejunitis; an entero-anastomosis was performed at the ileo-jejunal junction. The operation was followed by a long period of apparent good health. In 1945, or seventeen years later, the reappearance of heartburn and abdominal cramps was followed by the clinical picture of an "acute abdomen." The radiographic

examination showed the upper jejunum to be irregular, narrowed, tortuous; the upper jejunum and the duodenum were distinctly dilated and retained barium. At operation the roentgenographic findings were confirmed; the jejunum was diffusely scarred, the lumen contracted and the proximal bowel and duodenum and stomach abnormally dilated. A gastro-jejunostomy and a jejuno-jejunostomy were performed; the patient succumbed to the high intestinal obstruction and the extensive surgical procedures. Apparently in this case, in spite of the entero-anastomosis, the healing of the short circuited segmental jejunitis had resulted in scar tissue contraction and in high intestinal obstruction.

In Group D, where a high jejunitis is associated with an independent and similar lesion in the terminal ileum, the operation of choice is localized resection of the upper jejunal lesion and a short circuiting of the lower ileal lesion (ileo-transverse colostomy with transection of the proximal ileum above the diseased area). This present series includes three additional instances of combined lesions successfully operated by local resection of the jejunal affect and short circuiting of the terminal ileal segment, all of them successfully accomplished.

In summary it will be seen that surgical intervention in ileo-jejunitis is advocated both as an exploratory procedure and as a means of attack in those cases of high jejunitis with or without distal ileal involvement. In the localized or segmental forms of jejunitis, surgical intervention results frequently in restoration of health and intestinal function.

15 Ileo-Colitis—Combined Forms

BOTH ILEITIS and so called nonspecific or indeterminate colitis constitute diseases if not identical in nature, at least of the same family The etiology of neither disease is known both occur in young people, with the same even sex determination, both run the same general life span of extension and are signalized by such common complications as rectal suppurative phenomena, erythema nodosum, fever, secondary anemia and nutritive disturbances Both occur in pure form in the overwhelming proportion of cases but certain mixed forms must be recognized Thus severe universal ulcerative colitis will involve in about 24 per cent of the cases, the most terminal portion of the ileum This, however, does not constitute regional or terminal ileitis but is simply the backwash of the colitis through the ileo cecal valve into the reservoir of terminal ileum Such ileitis does not extend upward by skip lesions and does not form internal nor external fistulas On the other hand, true regional enteritis rarely crosses the ileo cecal valve but does persist proximal to the valve of Bauhin When the ileum is anastomosed to the colon as occurs in all short circuiting operations and in resections for ileitis, recurrences take place in the new terminal ileum but rarely in the apposed colon even though now the guardianship of the ileo cecal valve is no longer present In some instances the recurrence of ileitis at the free and open anastomosis has been followed for many years (in one case up to seventeen years) and yet when the anastomosis was taken down the transverse colon was free of disease sug

gestin, the fact that the colon is relatively immune to the "virus" of the ileitis

Relatively, yes, but not always so, since combined forms of the disease do occur, in this series of 306 cases of ileitis

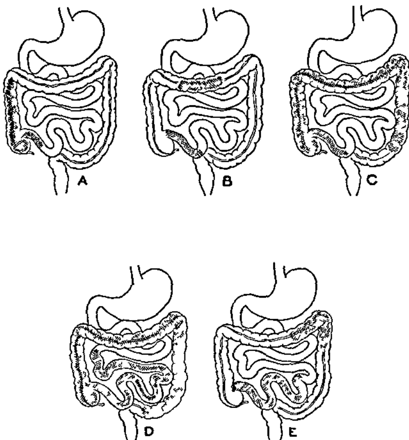


Fig 70—Combined Ileitis and Colitis (22 Cases) (A) terminal ileum and proximal colon (10 cases) (B) terminal ileum and transverse colon (2 cases) (C) terminal ileum and whole colon (except rectum) (6 cases) (D) ileum jejunum and whole colon (except rectum) (2 cases) (F) terminal ileum and distal colon (2 cases)

are included 22 cases of combined ileitis and colitis Of these 22 cases, 11 represent combinations of true terminal

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These findings of combined lesions were confirmed in 1936 by Crohn and Rosenak who cited 60 cases of regional ileitis, in 9 of which simultaneous involvement of the colon was found to exist Musick further described a case in



Fig 72—Regional Ileitis and Colitis Involving Cecum Ascending and Proximal Transverse Colon in a 21 Year Old Man At operation the extensive involvement of the colon was fully realized Ileo sigmoid ostomy with creation of temporary mucosal colostomy of proximal sigmoid

which 18 inches of ileum 3 inches of cecum and 3 inches of sigmoid were simultaneously involved An ileo ascending colostomy

right side, a Mikulicz

cessful outcome Pes

is with involvement

ileitis and various forms and distributions of ulcerative colitis, the other 11 cases are mixed types of diffuse ileitis and ileo jejunitis and variously distributed patterns of ulcerative colitis (fig 70) The sequence in the life history of the combined diseases is not known since when recognized



Fig 71 --Regional Ileitis at Onset Subsequent extension to ascending and transverse colon surgical resection recurrence in upper ileum and jejunum General health well preserved good working efficiency consistent gain in weight Only occasional flare up of mild diarrhea

both large and small bowel are already involved Actually, Colp as early as 1934 first pointed out the existence of a combined form of ileitis and colitis In 1935, Mixter reported a case of terminal ileitis with extension into the cecum In the discussion of Mixter's cases, Binney also quoted a case in which an extension of the process into the cecum caused perforation and a localized abscess

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which 18 inches of ileum 3 inches of cecum and 3 inches of sigmoid were simultaneously involved An ileo ascending colostomy was performed on the right side a Mikulicz procedure on the left colon with successful outcome Pessagno (1937) reported regional ileitis with involvement

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The most common form is constituted of those cases in which the terminal ileum is associated with a disease process involving the proximal colon, cecum and ascending colon up to the hepatic flexure (10 cases) (fig 73) Of equal frequency are mixed forms of terminal ileitis and transverse or distal colon involvement (10 cases) Finally



Fig 73—Combined Ileitis Ceciti and Ascending Colitis Result in restoration to perfect health

one notes 2 cases of great severity where the whole of the small intestine and the whole of the colon to the sigmoid are almost continuously involved It is of interest to note that the rectum and pelvic colon are rarely invaded the form of colitis under consideration is the segmental or regional form with proximal involvement For it is known that in regional colitis the parent lesion regularly occurs in the proximal colon and extends distally usually over the course of years (Crohn and Berg) The life cycle of the disease has been studied, the inflammatory process stops

of the cecum Pugh reported 9 cases of ileitis with evidence of extension of the pathologic process into the large bowel In 6 the cecum, in 2 the sigmoid and in one the transverse colon were implicated The parenthood of the combined form of the disease seems to rest in the terminal ileum Pemberton and Brown pointed out that if an ileo colostomy be performed for a combined lesion, at subsequent exploration the colonic lesion will be found healed, only the ileitis constituting the residual focus of the disease This is an astute observation which is amply *confirmed in the* life histories of several cases in this present series Clark and Dixon found that in 23 out of 44 cases of regional enteritis observed, the large bowel, mainly cecum and ascending colon were involved with the terminal ileum And yet, they distinctly say "The distal portion of the ileum appeared to be the original site of invasion of the disease in practically all cases" (figs 71 and 72)

Etiology

The age and sex distribution of combined ileo colitis is similar to that of the two independent diseases The age incidence ranged from 16 years to 56 years, the average or mean age being 28.5 years The sexes were evenly divided, 11 males and 11 females

The pathologic distribution over the anatomy of the two tracts is the most interesting feature but the various forms and combinations are so heterogenous as to make systematic classification difficult An attempt at classification may be made, however, as in table 19

TABLE 19—*Distribution of Combined Ileo Colitis*

	Cases
Terminal ileum and proximal colon	10
Terminal ileum and transverse colon	2
Terminal ileum and distal colon	[illegible]
Terminal ileum and whole or distal colon to sigmoid	6
Ileum and jejunum and whole colon	[illegible]
Total	[illegible]

that form of terminal ileitis which is characterized by mass formation and by multiple internal fistula formation The spleen was palpable in 2 cases, clubbing of the fingers occurred once in this group

Internal intestinal fistulas occurred in four instances, as demonstrated by x ray examination, one from ileum to

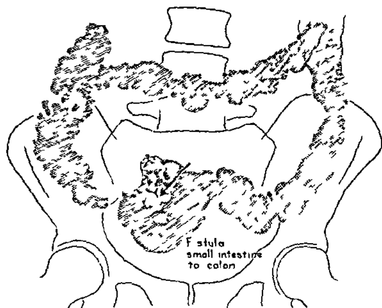


Fig 74—Fistula between Diseased Terminal Ileum and Pelvic Colon Fistula discernible as a fine line in the radiograph

the cecum, one to the transverse colon, two to the sigmoid (fig 74) Again internal fistulas from terminal ileum to other loops of small intestine such as characterize true terminal ileitis have not been noted In only one case was a fistula present to the anterior abdominal wall

Rectal complications such as mark both ileitis and ulcerative colitis are again present in this combined form as would be expected Perirectal suppurative fistulas and ischiorectal abscesses occurred in 9 of the 22 cases, a recto vaginal fistula in one instance Intestinal obstruction at the terminal ileum occurred once only in this group

or tarries for long periods at the sigmoid flexture, extending into the rectum rarely or only late in the course of an intractable and particularly virulent type of invasion and progression

That even the rectum is not immune is evidenced by the fact that in 2 of the fatal cases that succumbed after multiple and unsuccessful resections, the terminal phase was marked by severe proctitis Two other living cases have severe grades of proctitis, following unsuccessful surgical procedures

Clinical Features

Except for the greater severity of the disease, the combined forms of ileo colitis duplicate in general those of regional enteritis and of ulcerative colitis The general features are those of fever, which was present at some time in nearly all of the cases, again low grade and intermittent, present during the active phases of the disease, absent during remissions The temperature may reach as high as 104 F in exceptional cases, but usually varies between 101 and 102 F Malnutrition is extreme, losses of up to 50 or 65 pounds occurring in the more severe types of cases A mild leukocytosis (10,000 to 12,600) may be present with an abnormal increase of nonsegmental forms in the blood, indicating severe toxicity Secondary anemia is marked with hemoglobin values usually ranging between 60 and 80 per cent Sahli Exceptional hemoglobin readings of 30 and 55 per cent have been noted, the red blood cell count corresponding Sedimentation rate in the blood is usually moderately increased

Hypoproteinemia is unusual, for even in severe cases the total serum proteins average between 6 0 and 6 3 grams per 100 cc with only an occasional slight inversion of the albumin globulin ratio Occasional hypocalcemia has been observed

The Physical Signs

Rarely an abdominal mass is present, for the dispersion of the disease process in the ileum and colon differs from

tion was performed but within one and a half years a recurrence, severe in nature, initiated by a melaena was observed in the whole colon, including even the rectum This is an excellent example of a localized process of combined ileitis and colitis in which the recurrence involved the whole colon without recurrence in the residual ileum In a second case cited by Taylor the resection of a strictly localized ileitis involving only 30 cm of the terminal ileum recurred in three months with involvement of the whole colon with fatal termination

Medical Treatment

The medical treatment of the combined forms is not dissimilar to the care of ileitis or colitis namely bed rest, sunshine, bland nonroughage diet vitamin replacement by oral and parenteral route with the liberal use by injection of crude liver extract and vitamin B complex Parenteral use of plasma, protein hydrolysates, and multiple transfusions are highly to be recommended Of this series, 3 cases were not operated upon, one is well, spontaneously cured the other 2 are too extensively involved to allow for any surgical resection or short circuiting operation

Surgical Approach

The surgical approach to the cure of the disease is extremely varied and complicated and differs in each case depending upon the individual factors and the degree and extent of involvement of the various segments of large and small bowel

Four cases have had an ileo transverse colostomy with transection of the ileum performed thus short circuiting a circumscribed lesion involving the ileum and proximal colon One case is well, 2 have continued to do poorly because of persistence of the original disease the fourth has had extensive recurrences in the remainder of the colon

Resection of the original lesion in terminal ileum and proximal colon seems to have been the operation of choice

Prognosis

The prognosis in combined ileo colitis is poor, as might be expected where two such severe diseases are concurrently present The end results to date are as shown in table 20

TABLE 20—*End Results in Ileo Colitis*

	Cases
Well	7
Improved	2
Poor	9
Ceased	3
No follow up	1
Total	2

Again it is interesting to note that 7 cases are well Of these, only one case represents a spontaneous recovery under conservative management This was an instance of terminal ileitis with concurrent involvement of the transverse colon Under nonspecific protein therapy, using typhoid vaccine as an agent, clinical improvement was rapid, and eleven years later this man is apparently perfectly well and free of symptoms The recent x ray study shows a perfect mucosal pattern in the colon throughout, the terminal ileum remains slightly distorted in outline

The remaining 6 cases which are "well" represent successful surgical resections or short circuiting procedures

Two cases are improved 9 cases are classified as unimproved Of these 9 instances of poor results, 5 represent surgical failures usually after multiple attempts, 4 have done badly because of such an extensive involvement of ileum, jejunum, and colon as to preclude any radical surgical approach

Three further cases have ceased, 2 of them after multiple resections until only an ileo sigmoidostomy remained followed by recurrences in rectum and upper small bowel The remaining case died of uremia, associated with multiple renal calculi and kidney parenchymatous damage

Taylor describes a case with involvement of the terminal ileum, ascending colon up to the hepatic flexure A resec

vation Cases successfully operated elsewhere would naturally have no necessity to seek further help, they are probably numerous throughout this country and elsewhere, where the combined types of ileitis and colitis are recognized and surgeons of ability are willing to devise some surgical procedure which fits the individual pattern and gives promise of fruition Such a successful outcome is seen in the case of Musick, in which ileum, cecum and sigmoid were all involved An ileo ascending colostomy was employed to short circuit the ileo-cecal area of disease a Mikulicz procedure was utilized to resect the area in the sigmoid The man was back at work within three month restored to health

In a very recent publication the involvement of the ileum and jejunum secondary to extensive ulcerative colitis is stressed (Olsan and Sussman) This observation confirms the occasional case, rare fortunately, in which one sees involvement of the jejunum in a very serious type of ulcerative colitis The widespread inflammatory invasion should be regarded as essentially colitis and not true ileitis or jejunitis

in most instances In this series, 9 cases had been submitted to such a procedure with greatly varying results Three of the 9 cases so operated are well today, many years after the original procedure Two have died as a result of extensive recurrences with subsequent multiple operations and eventually involvement of the rectum The extension of the process to the rectum or to the upper jejunum always *marks the terminal stage of the disease*

The remaining 4 cases that underwent resection as an initial procedure have fared badly because of extensive recurrences in colon mainly, one also in jejunum, but have not been subjected to further surgical procedures

Four cases were submitted to ileo sigmoidostomy One is well, one died of uremia some months after operation, 2 have done poorly, and are awaiting resection at some *future date*

Two cases remain as instances of extreme surgical necessities One has had a high ileostomy as an attempt at a life saving procedure one had had elsewhere a jejuno sigmoidostomy in an attempt to short circuit all of the ileum and all of the colon down to the sigmoid The latter is a particularly poor result with marked hypoproteinemia and malnutrition All in all, the results are not good Five *well out of 22 cases is not very promising* However, it should be remembered that most of these cases were referred because of the disappointment over the results of initial surgical attack previously performed elsewhere and lacked success, although the procedures had been carried out by most competent surgeons Of the cases in which the diagnosis and surgical indications were solely in my own hands from the initiation (7 cases) 4 are well, one has died, one is a poor surgical result and one is awaiting further resection after an ileo sigmoidostomy with good promise Perhaps these 7 cases give a more true picture of the eventual prognosis The remainder of the series hardly constitute a basis of prognostication since they had already suffered the handicap of being failures before coming under obser

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